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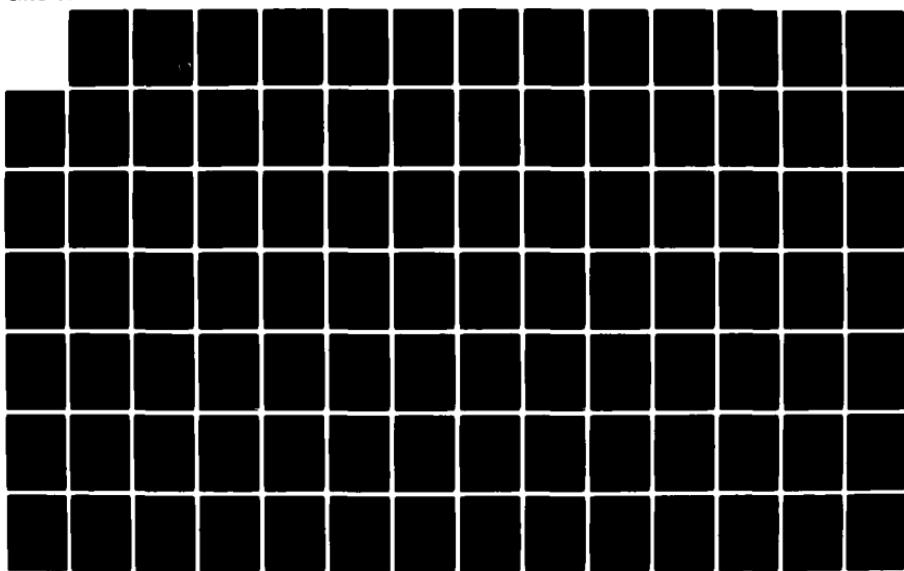
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CYANAMID CO BOUND BROOK NJ DISCOVERY RESEARCH DEPT
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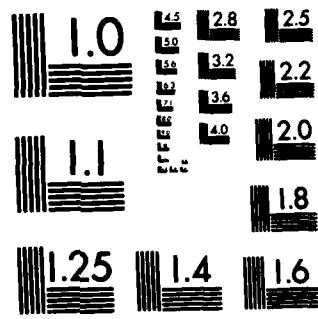
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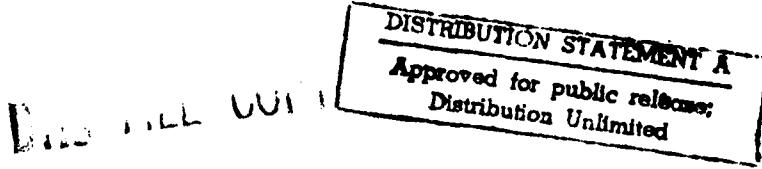
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THE OFFICE OF NAVAL RESEARCH

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BY: A.G.MOHAN,S.S.TSENG,M.M.RAUHUT,F.J.ARTHEN,R.G.DULINA
V.M.KAMHI,D.E.MCKAY,R.J.MANFRE,J.D.OFELDT AND L.S.VIZCARRA

DISCOVERY RESEARCH DEPARTMENT
CHEMICAL RESEARCH DIVISION
AMERICAN CYANAMID COMPANY
BOUND BROOK,N.J.
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AQUEOUS PEROXYOXALATE CHEMILUMINESCENCE

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AQUEOUS PEROXYOXALATE CHEMILUMINESCENCE

I. SUMMARY

An investigation of peroxyoxalate chemiluminescence in aqueous solution has provided a reaction system with a quantum yield of 7.2%, 1800 times higher than had been reported at the start of this project. Two major discoveries led to this improved efficiency: 1. the discovery that certain rubrene derivatives were highly efficient in aqueous chemiluminescent reactions and 2. the discovery that the addition of certain surfactants, especially non-ionic and anionic types, improved the quantum yield by as much as seven times. Additional improvements in efficiency were obtained by the discovery of new, highly efficient oxamides.

The most efficient aqueous system discovered is the reaction of bis-[N-2-(N'-methyl-2'-pyridinium)ethyl-N-trifluoromethylsulfonyl]-oxamide, bis-trifluoromethanesulfonate with hydrogen peroxide in the presence of sulfonated rubrene as the fluorescer, providing a quantum yield of 7.2%. At a .04 M concentration of the oxamide, the light capacity was found to be 62 lumen hours per liter. A system using bis-hexylrubrene in an emulsified organic solvent was also highly efficient, providing a quantum yield of 8.3% in aqueous media.

During the course of this work a record high chemiluminescence quantum yield of 34% in an organic solvent was established for non-enzymatic chemiluminescent reactions by the discovery of the highly efficient oxamide, bis-[N-(2,4,5-trichlorophenyl)-N-trifluoromethanesulfonyl]oxamide.

II. INTRODUCTION

The American Cyanamid Company has conducted research on chemiluminescence since 1961 (1,2), with the objective of exploiting the inherent advantages of chemically produced light through the discovery of practical marking and illumination systems. The attractive potential of chemical light is based on:

1. A high theoretical light capacity of 173,000 lumen-hr per liter, equivalent to the light output of a 40-watt incandescent bulb burning continuously for 2 weeks (2). The potential for high light capacity makes chemiluminescence an attractive target for research directed to the development of systems for portable lighting, power failure emergencies and other applications where the use of electrical power is inconvenient or impossible.
2. Chemiluminescence is cold light. Since heat and flame are absent, chemical light systems can be used in areas where conventional hot lights would cause fire or explosion. Examples of such situations would include aircraft and shipboard accidents, repair of gas transmission lines, and in coal mines.
3. Reliability through long shelf life. Conventional storage batteries gradually lose energy even in storage. Chemical light systems, in principle, can have indefinite storage lifetimes.

Chemiluminescent reactions with the efficiency necessary for practical use were unknown at the beginning of Cyanamid's research program. Even the fundamental knowledge required for the discovery of practical reactions was unknown.

Following initial feasibility studies (3), a detailed mechanism study was begun in 1963 under contract with the Office of Naval Research to obtain the basic knowledge required to design practical chemiluminescent reactions. This program was successful (4) and led to the discovery of practical chemical light systems under subsequent contracts with the Naval Ordnance Laboratory (5,6). As a direct result of these programs, the light output was increased more than 1600 times (7). Under a later contract with the Naval Weapons Center, the causes of decreasing efficiency with increasing reactant concentration were determined, and a new record high light capacity of over 900 lumen hours per liter was attained (8). Concurrent with the later contracts, Cyanamid conducted a program which developed one of the more efficient systems into a practical commercial product, the Cyalume chemical lightstick. This product is currently in wide use throughout the world for a variety of military and civilian applications. In a more recent contract with the Office of Naval Research the effect of key reaction variables was investigated (9). This led in a later program to the development of a new class of highly efficient oxalic acid derivatives, the triflyl oxamides. A record high chemiluminescent quantum yield of 34% was obtained for

one of the oxamides in this series (10).

The feasibility of a water-based chemiluminescent system was initially investigated under a program supported by NASA's Goddard Space Flight Center (11). Such a system would have several advantages over the current Cyalume lightstick where the organic solvent constitutes most of the weight and volume. It has been estimated that a 4-gram tablet containing only the active ingredients could produce more than 10 times the light output of the Cyalume green lightstick but will weigh only 7% as much (12). The practical advantages of such a tablet are:

1. high light density (light output per unit weight of system)
2. rapid activation by water
3. long shelf life when protected against humidity
4. low toxicity
5. absence of fire hazard

These criteria will make water-activated chemical light particularly suited for those applications where conventional lights might create a fire or explosion hazard and where portability or small storage area are required. Water for activation will be available for many applications from sea water or waste water as well as from taps or streams.

Applications for the water-based system will include:

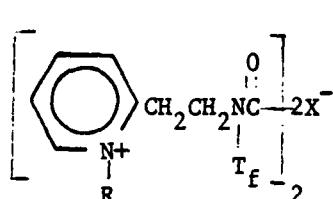
1. lifeboat and raft marking for search and rescue; automatic lighting for life vests
2. emergency lighting for ships and aircraft, especially in confined spaces where fuel fumes may be present
3. marking and lighting for military units in the field.

III. INVESTIGATION OF NEW CHEMILUMINESCENT SYSTEMS

A. RESULTS

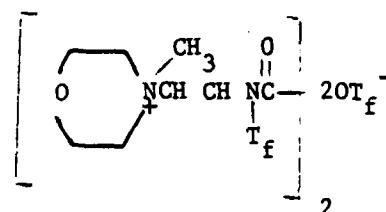
1. Aqueous Reactions

Although efficient chemiluminescent reactions have been known for some time in non-aqueous solvents, no efficient aqueous reactions have been reported until the present study. The oxamide PETQ, 1, was found to give a quantum yield of 1.45% when treated with hydrogen peroxide in the presence of a water-soluble fluorescent compound, rubrene sulfonate, 3. An even more dramatic effect was found when a non-ionic surfactant was added to this reaction mixture. The efficiency increased over four-fold to a quantum yield of 7.00%. The use of a solvent, cyclohexane, in a similar reaction with the oxamide METQ, 4, gave quantum efficiencies exceeding 8%.

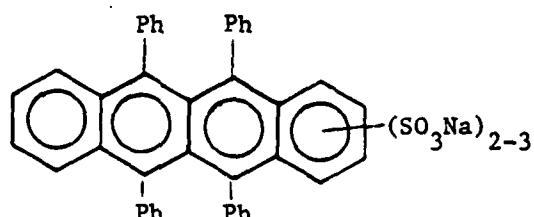
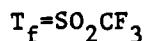


1 PETQ: R=CH₂, X=OT_f

2 PETH: R=H, X=Cl



4 METQ



3

A number of variables have major effects on the efficiency of this reaction: the structure of both the oxalic acid derivative and the fluorescer, the concentrations and structure of the surfactant, the pH of the medium, and a variety of other factors. The results of experiments investigating these variables are summarized in the paragraphs which follow. The syntheses of the new fluorescers and oxalic acid derivatives used in these reactions is described in Sections 3 and 4.

The data summarized in Table 1 show the marked improvement obtained by the addition of the surfactant to the chemiluminescent reaction mixture with two different oxamides, PETQ and METQ.

TABLE 1: EFFECT OF SURFACTANT ON THE CHEMILUMINESCENCE EFFICIENCY OF TRIFLYL OXAMIDES

OXAMIDE	SURFACTANT CONC.	QYX100	Lc	T.75	k1
PETQ	NONE	1.45	11.6	6.0	.167
PETQ	.001M	7.00	62.3	5.8	.129
METQ	NONE	0.64	4.9	1.6	.699
METQ	.001M	4.48	36.3	2.3	.710

1. Chemiluminescent reactions contained .04 M oxamide, .01 M rubrene sulfonate, 1.75 M hydrogen peroxide and the indicated concentration of the nonionic surfactant, Deceresol NI.

2. Pseudo-first order rate constant (in 1/min) for light decay.

Note: In all the tables QY indicates the quantum yield in einsteins per mole of reactant, Lc is the light capacity in lumen hours per liter of reaction solution, and T.75 is the time required for 75% of the total light to be emitted.

The data in the table also show that the addition of a non-ionic surfactant, "Deceresol NI", gives a substantial improvement in efficiency when added to the reaction. Figures 1 and 2 indicate that no significant change in spectral distribution is evident when the surfactant is present. Figure 3 graphically demonstrates the improvement obtained on addition of the surfactant. A comparison of the effect of the NI surfactant on two related oxamides, PETQ and PETH (2), is shown in Table 2. Again a significant difference in rate of emission is evident between the two oxamides, but the addition of tetrahydrofuran (THF) to the PETH system gave essentially no change. Qualitative experiments had given some indication of enhanced luminescence, but the quantitative data rule this out. Additional studies will be required to clarify the mechanism by which the efficiency is improved.

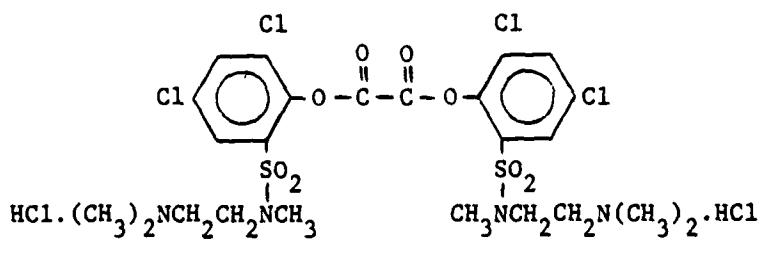
TABLE 2: CHEMILUMINESCENCE EFFICIENCY OF 2-PYRIDYLETHYL TRIFLYLOXAMIDES

OXAMIDE	ADDITIVE	QYx100	Lc	T.75	k1
PETQ	.001M NI	7.19	62.3	6.6	137
PETQ	.001M NI	6.42	55.7	10.9	93.9
PETH	.001M NI	7.02	60.2	21.0	50.6
PETH	.001M NI	6.47	55.5	23.3	51.7
PETH	.001M NI+THF	7.32	60.6	23.6	50.1
PETH	.001M NI+THF	6.52	54.1	27.5	47.3

1. Chemiluminescent reactions contained .04 M oxamide, the indicated concentration of Deceresol NI surfactant, .01 M rubrene sulfonate and 1.75 M hydrogen peroxide.
2. Pseudo-first order rate constant (in 1/min) for light decay.
3. See Table 1 for heading definitions.

The spectral distributions for the chemiluminescent reactions with sulforubrene are illustrated for PETH and PETQ in Figures 4 and 6, respectively. The intensity decay for PETH is shown in Figure 5, and the effect of surfactant on the intensity decay of the PETQ reaction is illustrated in the two curves in Figure 7.

The oxalate ester SAPO was one of the earliest compounds found to have any significant efficiency in water, albeit only 0.004% efficient using HPTS (8-hydroxy-3,5,6-pyrenetrisulfonate) as the fluorescer. The chemiluminescent reaction with the sulforubrene-surfactant system was repeated with SAPO, and a substantial increase in efficiency was found. A comparison of the performance of SAPO with three triflyloxamides is given in Table 3. The much longer lifetime found with SAPO in this reaction contrasts with the shorter lifetimes of the three triflyloxamides. This may be in part due to the low solubility of SAPO in water. The intensity decay curve for the SAPO system is illustrated in Figure 8. No change in the spectral distribution was evident in this system (see Figure 9).



SAPO

TABLE 3: COMPARISON OF PERFORMANCE OF SAPO WITH TRIFLYLOXAMIDES

COMPOUND	QYx100	T.75	Lc
SAPO	4.48	312	32.6
METQ	4.48	2.3	36.3
PETQ	7.19	6.6	62.3
PETH	6.47	23.3	55.5

1. Chemiluminescent reactions contained .04 M of the oxalic acid derivative, .001 M Deceresol NI surfactant, .01 M sulforubrene and 1.75 M hydrogen peroxide.

2. See Table 1 for heading definitions.

In general, all of the water-soluble oxalic acid derivatives synthesized in this program gave light emission in water in the presence of a fluorescer and hydrogen peroxide. However, some of these compounds gave either very weak or bright and short-lived reactions in water. In these cases quantitative determination of the efficiency was not carried out. In order to obtain meaningful and reproducible results only those compounds which gave good qualitative chemiluminescence were evaluated quantitatively. As mentioned above, a number of the early oxalic acid derivatives were evaluated against the commercially available fluorescer 8-hydroxy-1,3,6-pyrenetrisulfonate (HPTS). Some of these same compounds were evaluated with sulforubrene as the fluorescer. Table 4 summarizes the performance of several of these compounds compared to two standards (METQ and PETQ).

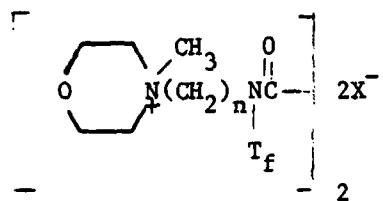
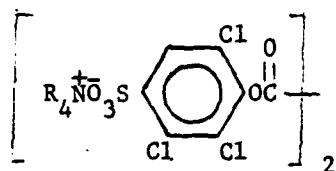
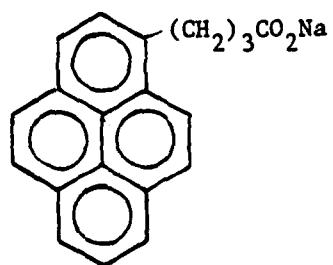
TABLE 4: CHEMILUMINESCENCE PERFORMANCE OF OXALIC ACID DERIVATIVES WITH HPTS OR SULFORUBRENE IN WATER

COMPOUND	FLR	CONC., M	QYx100	T.75	Lc
METQ (4)	HPTS	.04	.01	4.0	.1
	RS	.01	.85	.1	.4
(5)	HPTS	.06	.008	6.0	.1
PETQ (1)	HPTS	.02	.002	17	.01
	RS	.04	1.6	6	13
(6)	HPTS	.025	.01	41	.07
SAPO	HPTS	.0068	.003	2.5	.005
	RS	.04	.70	232	5
(7)	RS	.05	.02	.1	.22

1. Chemiluminescent reactions contained the indicated concentrations of the oxalic acid derivatives, .0068 M HPTS or .01 M sulforubrene, 1.75 M hydrogen peroxide, and .0012 M sodium salicylate in water.

2. See Table 1 for heading definitions.

Structures For Table 4

5 n = 2, X = BF₄⁻6 MPTQ: n = 3, X = OT₄⁻78

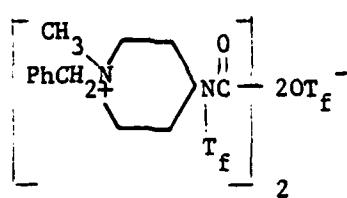
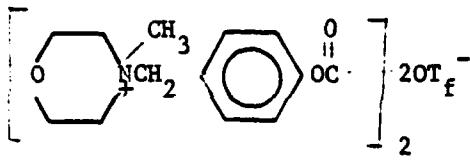
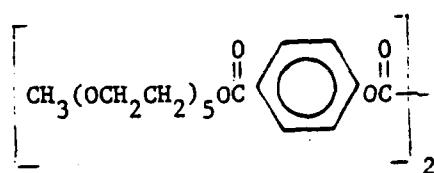
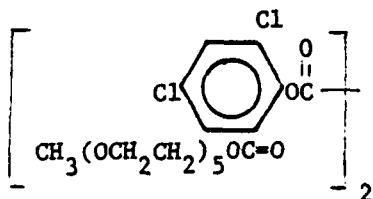
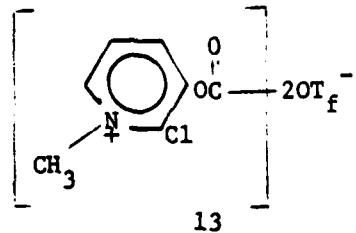
A number of the more efficient oxalic acid derivatives were evaluated as summarized in Table 5. Only those compounds which showed significant light emission in qualitative tests were evaluated quantitatively.

TABLE 5: EVALUATION OF WATER SOLUBLE OXALIC ACID DERIVATIVES IN THE SULFORUBRENE-SURFACTANT CHEMILUMINESCENT REACTION

OXALIC ACID DERIVATIVE	QYx100	T.75	Lc
METQ	4.76	1.2	43.2
METQ-HPTS	.03	8.9	.2
METQ-FLR <u>8</u>	.78	5.0	5.6
MPTQ <u>6</u>	.35	4.0	1.1
PETQ	7.05	5.9	62.6
PETH	7.31	24	60.8
BPTQ <u>9</u>	4.49	1290	35.2
SAPo	4.41	312	32.6
<u>10</u>	1.15	7.3	8.8
<u>11</u>	.18	3.3	1.8
<u>12</u>	.44	5.5	3.5
<u>13</u>	.05	6.0	.4

1. Chemiluminescent reactions contained .04 M of the oxalic acid derivative, .01 M sulforubrene, 1.75 M hydrogen peroxide, .0012 M sodium salicylate and .001 M Deceresol NI surfactant. The structures of the oxalic acid derivatives are shown on the following page.
2. The indicated fluorescers were used in these reactions.
3. The concentration of oxalate ester 11 was .046 M.
4. See Table 1 for heading definitions.

Structures For Table 5

9 BPTQ10111213

A number of water-soluble rubrene derivatives (14, 15 and 16.) were prepared since the sulfo rubrene gave such high efficiency in the aqueous chemiluminescent reaction with METQ. Table 6 summarizes the performance and spectral properties of these fluorescers.

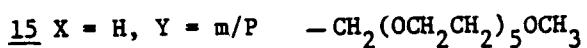
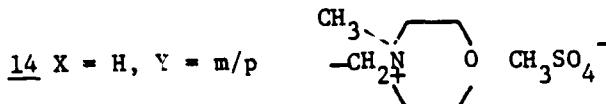
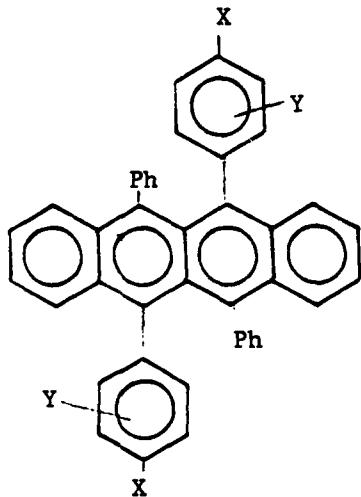
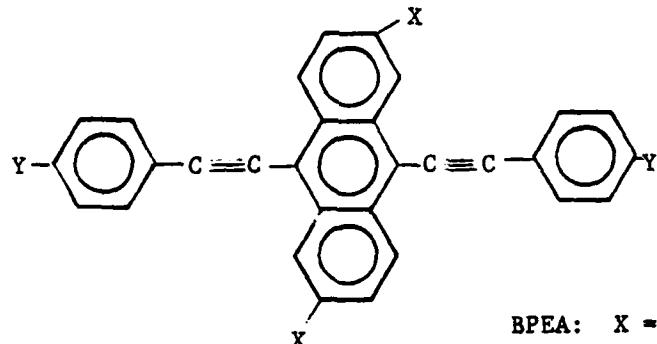


TABLE 6: CHEMILUMINESCENCE PERFORMANCE OF WATER-SOLUBLE RUBRENE DERIVATIVES

COMPOUND	max	P	QYx100	T.75	Lc
<u>14</u>	575nm	.555	2.91	10.1	26.4
<u>15</u>	600	.510	3.61	6.4	29.4
<u>16</u>	620	.309	3.52	10.3	17.6

1. Chemiluminescent reactions contained .01 M of the fluorescer, .04 M METQ, 1.75 M hydrogen peroxide and .001 M Deceresol NI surfactant.
2. P is the photopic factor, a measure of the sensitivity of the human eye to the spectral distribution of the emitted light.
3. See Table 1 for heading definitions.

Several water-soluble derivatives of BPEA were also prepared (17, 18, 19, and 20). The spectral properties and performance of these fluorescers are summarized in Table 7.



BPEA: X = Y = H

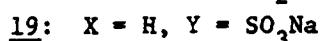
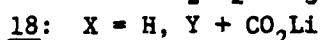
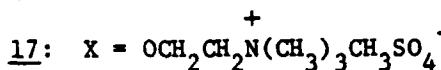


TABLE 7: CHEMILUMINESCENCE PERFORMANCE OF WATER-SOLUBLE BPEA DERIVATIVES

COMPOUND	max	P	QYx100	T.75	Lc
<u>17</u>	530	.743	.44	4.7	5.3
<u>18</u>	640	.221	.04	4.2	.2
<u>19</u>	515	.680	.62	4.2	6.2
<u>20</u>	570	.552	.57	3.7	6.3

1. Chemiluminescent reactions contained .003 M fluorescer, .04 M METQ, 1.75 M hydrogen peroxide and .001 M Deceresol NI surfactant.

2. P = photopic factor.

3. See Table 1 for heading definitions.

Two water-soluble pyrene derivatives have been prepared (21 and 22). The performance of these fluorescers is summarized in Table 8.

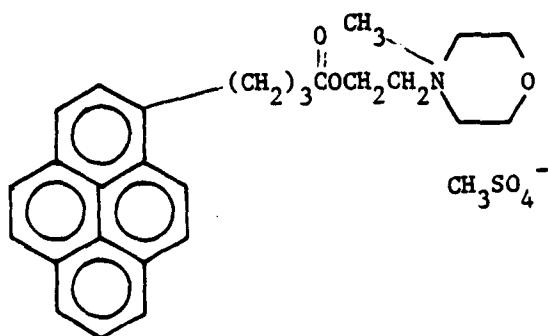
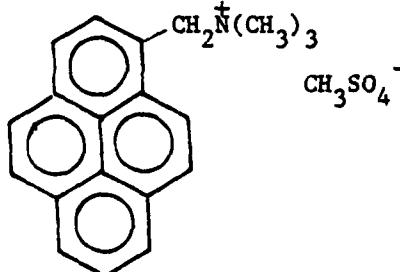
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TABLE 8: CHEMILUMINESCENCE PERFORMANCE OF WATER-SOLUBLE PYRENE DERIVATIVES

COMPOUND	max	P	QYx100	T.75	Lc
<u>21</u>	485	.398	.88	3.7	5.3
<u>22</u>	485	.422	.03	11.2	.2

1. Chemiluminescent reactions contained .04 M METQ, 1.75 M hydrogen peroxide, .001 M Deceresol NI surfactant, and .01 M of the fluorescer.

2. P = photopic factor.

3. See Table 1 for heading definitions.

The sodium salt of 1-pyrenebutanoic acid, 8, was prepared by neutralization of the acid with sodium hydroxide. It also gave slightly stronger blue chemiluminescence in water than HPTS and was about equal to 22.

Table 9 summarizes a set of experiments carried out with a solvent-emulsified system using fluorescers which are not soluble in water.

TABLE 9: EFFICIENCY OF FLUORESCERS IN WATER/CYCLOHEXANE EMULSION

FLUORESCER	QYx100	T.75	Lc
BPEA	.12	11.5	1.1
1-Chloro-BPEA	.12	8.0	1.3
2-Me-BPEA	.45	10.8	4.9
2-Et-BPEA	1.00	9.5	10.4
Bis-Octyl-BPEA <u>23</u>	.79	8.7	8.5
Rubrene	6.26	9.7	59.4
Tetrabromorubrene <u>27a</u>	6.74	9.3	46.7
Bis-hexylrubrene <u>28</u>	8.28	11.8	60.8
	8.02	14.0	59.9
Bis-dodecylrubrene <u>29</u>	6.78	10.9	51.1
	6.78	11.1	50.2

1. Chemiluminescent reactions contained .003 M of the BPEA derivatives, .01 M of the rubrene fluorescers, .04 M METQ, 1.75 M hydrogen peroxide and .001 M Deceresol NI surfactant in a solvent mixture of 82% water and 18% cyclohexane (by volume).

2. See Table 1 for heading definitions.

The spectral distribution from the rubrene emulsified system is illustrated in Figure 10 and the intensity decay curve in Figure 11. The spectral distributions from the chemiluminescent reactions of BPEA and its derivatives in the emulsion systems are shown in Figures 11 and 12. The intensity decay curves for BPEA and its alkyl derivatives in the solvent-emulsified system are illustrated in Figure 14.

A variety of surfactant structural types; nonionic, cationic and anionic were evaluated in the aqueous chemiluminescent system with the oxamide METQ and sulforubrene as the fluorescer. The data is summarized in Table 10.

TABLE 10: EFFECT OF SURFACTANT STRUCTURE ON THE EFFICIENCY OF THE METQ/SULFORUBRENE CHEMILUMINESCENCE SYSTEM

Surfactant	Structure		QYx100	T.75	Lc
<u>Nonionic</u>					
Deceresol NI	Nonylphenol+ 9	E.O.	4.48	2.3	36.3
Tergitol NP-4	" 4 "		4.28	1.9	37.0
"	" 4 "		4.40	2.6	37.6
" NP-6	" 6 "		4.28	1.5	37.6
"	" 6 "		4.07	1.5	35.8
" NP-7	" 7 "		3.95	1.0	34.0
"	" 7 "		3.68	1.4	31.7
" NP-10	" 10 "		4.27	1.2	38.7
"	" 10 "		4.03	1.6	36.5
<u>Anionic</u>					
Dowfax 2AI	Disulfodiphenyloxide		3.03	0.9	27.4
"	"		3.21	0.9	29.0
Alipal EP120	Ammonium salt of sulfate ester of NP+E.O.		3.02	1.0	27.9
Aerosol OT	Na dioctyl sulfo-succinate		3.18	1.4	29.0
Na Dodecylsulfate			3.50	1.4	32.0
			1.56	1.9	13.7
<u>Cationic</u>					
Dodecyltrimethylammonium Chloride			1.06	1.8	9.1
			0.59	1.3	5.1

1. Chemiluminescent reactions contained .04 M METQ, .01 M sulforubrene, 1.75 M hydrogen peroxide, and approximately 1% of the indicated surfactants in water.

2. E. O. = ethylene oxide groups.

3. See Table 1 for heading definitions.

Table 11 illustrates the effect of varying the surfactant concentration on the efficiency of the METQ/sulforubrene system. The highest quantum yield was found at the lowest surfactant concentration, .001 M.

TABLE 11: EFFECT OF NI SURFACTANT CONCENTRATION ON THE EFFICIENCY OF THE METQ/SULFORUBRENE SYSTEM

SURFACTANT CONC.	QYx100	T.75	Lc
None	0.75	1.7	6.0
.001M	4.48	2.3	36.9
.028	3.15	0.7	26.4
.029	3.51	0.7	29.4
.054	3.02	1.0	25.4
.057	3.89	0.4	32.7
.057	3.80	0.7	31.9
.089	3.87	0.8	32.5
.089	3.81	0.9	32.0

1. Chemiluminescent reactions contained the indicated concentrations of Deceresol NI, .04 M METQ, .01 M sulforubrene, and 1.75 M hydrogen peroxide in water.

2. See Table I for heading definitions.

Table 12 summarizes the effect of variation of the sulforubrene concentration on the chemiluminescence efficiency of the METQ-surfactant system. The highest efficiency was found at the highest concentration of the fluorescer, .05 M. This concentration is an order of magnitude higher than the optimum concentrations found for the organic solvent-based systems. Excessive foaming prevented the use of higher levels of the fluorescer. Visually it was noted that the sulforubrene was substantially more stable to photoxidation in the aqueous-surfactant chemiluminescent reaction than in organic solvents.

TABLE 12: EFFECT OF SULFORUBRENE CONCENTRATION ON CHEMILUMINESCENCE EFFICIENCY OF METQ WITH NI SURFACTANT

SULFORUBRENE CONC.(Mx100)	QYx100	T.75	Lc
.01	.10	3.2	1.0
.01	.10	3.6	1.0
.10	1.13	2.8	11.3
.10	.97	3.3	9.8
1.0	3.28	1.3	28.9
1.0	3.46	1.1	30.6
5.0	3.78	1.1	23.2

1. Chemiluminescent reactions contained .04 M METQ and .001 M "Deceresol NI" surfactant. Hydrogen peroxide concentration was 1.75 M.

2. See Table 1 for heading definitions.

As might be expected, the pH of the solution should have a substantial effect on the efficiency and on the rate of light decay. Table 13 indicates that in buffered systems the overall efficiency of the METQ/sulforubrene/NI system is markedly affected by the pH of the medium. The highest efficiency was found at the lowest pH, and the lowest efficiency was found at the highest pH. A general trend of increasing rate of light decay was also apparent with increasing pH. This increase in decay rate is probably due to the increase in OOH ion concentration with increasing pH. A comparison of the intensity-time curves at three pH values is illustrated in Figure 8. Again the improved performance at the lower pH is clearly evident, with the highest efficiency being found at pH 3.

TABLE 13: EFFECT OF PH ON CHEMILUMINESCENCE EFFICIENCY OF METQ

pH	QYx100	Lc	T.75	k1
3.0	3.30	28.7	1.7	1.22
3.9	2.44	21.5	1.1	1.56
6.7	0.26	2.5	1.0	1.60
8.4	0.11	0.9	1.2	1.85

1. Chemiluminescent reactions contained .04 M METQ, .01 M rubrene sulfonate, .001 M NI surfactant and 1.75 M hydrogen peroxide. Solutions were buffered at the indicated pH values.

2. Pseudo first order rate constant (in l/min.) for light decay.
 3. See Table 1 for heading definitions.

The replacement of water with deuterium oxide in the METQ-sulforubrene chemiluminescent reaction actually reduced the quantum yield and increased the rate of light decay by about 30% (see Table 14). This suggests that the competitive processes which reduce the quantum yield are enhanced in the deuterium oxide. An enhanced hydrolysis of the oxamide in the isotopic solvent could explain these results.

TABLE 14: SOLVENT ISOTOPE EFFECT ON THE METQ-SULFORUBRENE REACTION WITH NI SURFACTANT

SOLVENT	QYx100	T.75	Lc	k
Water	4.48	2.3	36.9	.710
Deuterium Oxide	1.87	.7	18.2	.918
	2.27	.8	22.2	.970

1. Chemiluminescent reactions contained .04 M METQ, 1.75 M hydrogen peroxide, .01 M sulforubrene and .001 M Deceresol NI surfactant.

2. Pseudo-first order rate constant (in l/min) for light decay.
 3. See Table 1 for heading definitions.

A study of the METQ-HPTS was carried out to ascertain the effect of reaction variables on the chemiluminescence efficiency. Variation of the hydrogen peroxide concentration from 1.0 to 2.25M had no effect on quantum yield, but at concentrations above 5.0M both the quantum yield and lifetime were substantially reduced (see Table 15). The effect of the sodium salicylate catalyst concentration was also studied (Table 16); within the range .001 to .01M the quantum yield of the METQ-HPTS system remained at the maximum (.01%). Above this range both the efficiency and the lifetime decreased, presumably due to catalysis of the competitive base-catalyzed hydrolysis reaction. Below this range the quantum yield also decreased somewhat, but the lifetimes of the reactions were longer, as expected.

TABLE 15: EFFECT OF HYDROGEN PEROXIDE CONCENTRATION ON PERFORMANCE OF METQ-HPTS SYSTEM

HYDROGEN PEROXIDE

CONC. M

	QYx100	T.75	Lc
1.00	.007	19	.079
1.50	.007	18	.079
1.75	.008	17	.086
2.00	.007	20	.084
2.25	.007	15	.078
5.00	.005	4	.053
7.50	.003	2	.035
10.0	.001	1	.009

1. Chemiluminescent reactions contained .040 M METQ, .0068 M HPTS and .0012 M sodium salicylate catalyst.

2. See Table 1 for heading definitions.

TABLE 16: EFFECT OF THE CONCENTRATION OF SODIUM SALICYLATE CATALYST
ON THE METQ-HPTS CHEMILUMINESCENT REACTION

[NaSal] Mx1000	QYx100	T.75	Lc
100.	.003	1	.033
50.0	.006	2	.072
10.0	.008	8	.087
7.50	.008	9	.097
6.00	.008	10	.097
5.50	.008	13	.097
5.00	.009	12	.098
4.75	.009	10	.101
4.50	.009	11	.103
4.25	.010	11	.116
4.00	.008	13	.091
2.50	.007	12	.082
1.00	.007	18	.078
.500	.007	18	.078
.010	.007	24	.081
.005	.006	20	.074
.001	.006	18	.074

1. Chemiluminescent reactions contained 1.50 M hydrogen peroxide 0.0404 M METQ, .0068 M HPTS and the indicated concentrations of sodium salicylate (NaSal).

2. See Table 1 for heading definitions.

Qualitative studies were undertaken to investigate the effect of a variety of additives on the chemiluminescence of the METQ-HPTS system. The results of these experiments are summarized in Table 17.

TABLE 17: EFFECT OF ADDITIVES ON THE CHEMILUMINESCENCE OF
THE METQ-HPTS REACTION IN WATER

ADDITIVE	PROPERTY	QUALITATIVE EFFECT ON CHEMILUMINESCENCE
Potassium Persulfate	Strong oxidant	No effect
Copper(II) Chloride	Catalyst for dioxetane decomposition	Decreased
Sodium EDTA	Strong chelater	No effect
Silica gel or Alumina	Surface active solid	Slight increase
3A Molec.Sieves	Surface active solid	Decreased
Oxalic Acid	Strong acid quencher	Decreased
Ethyl Benzoate or Ethanol	OH radical scavenger	No effect
Potassium Carbonate	Base	Increased, lifetime reduced

1. Chemiluminescent reactions were carried out by adding a 1.5M solution of hydrogen peroxide to a solid mixture of METQ and HPTS. A small quantity of the additive was then added to the emitting reaction.

FIG.1:SPECTRAL DISTRIBUTION METQ/SULFORUBRENE

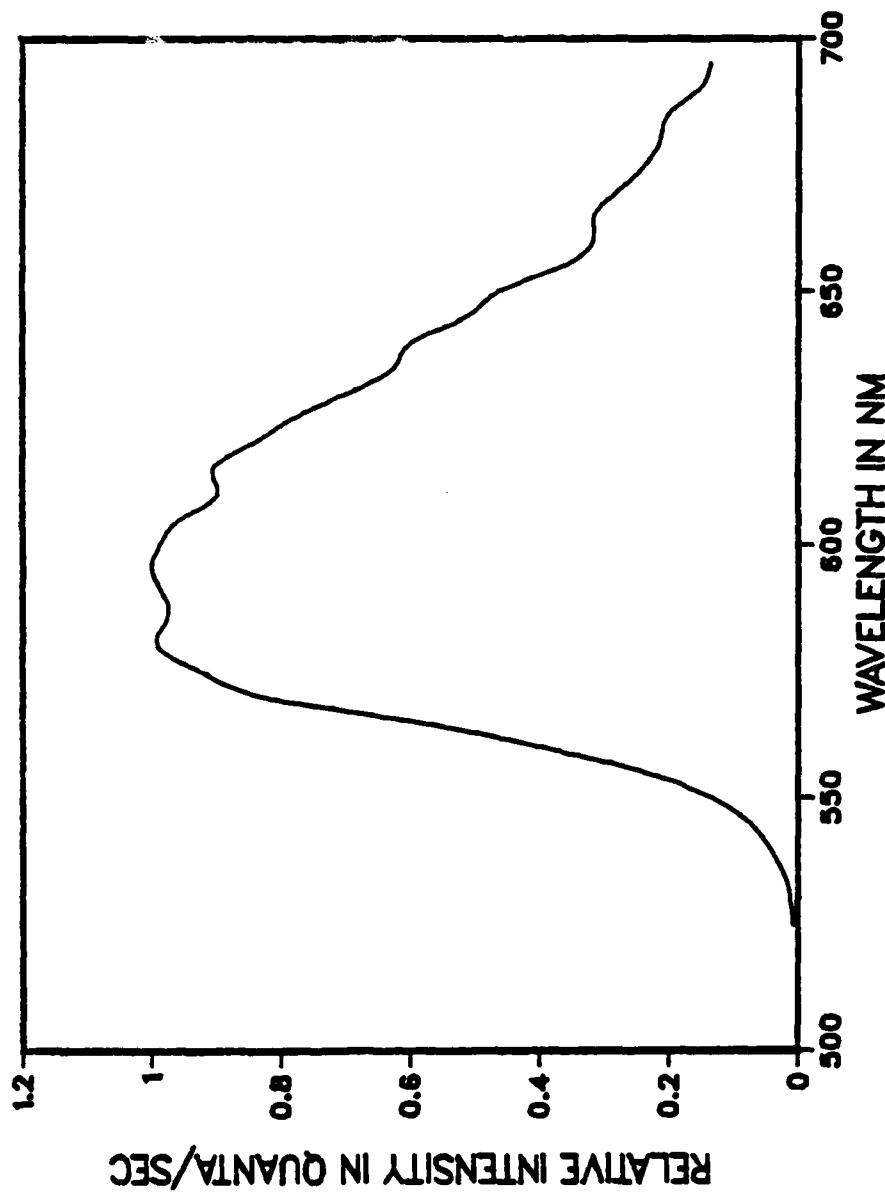


FIG.2: SPECTRAL DISTRIBUTION: METQ/SULFORUBRENE/NI

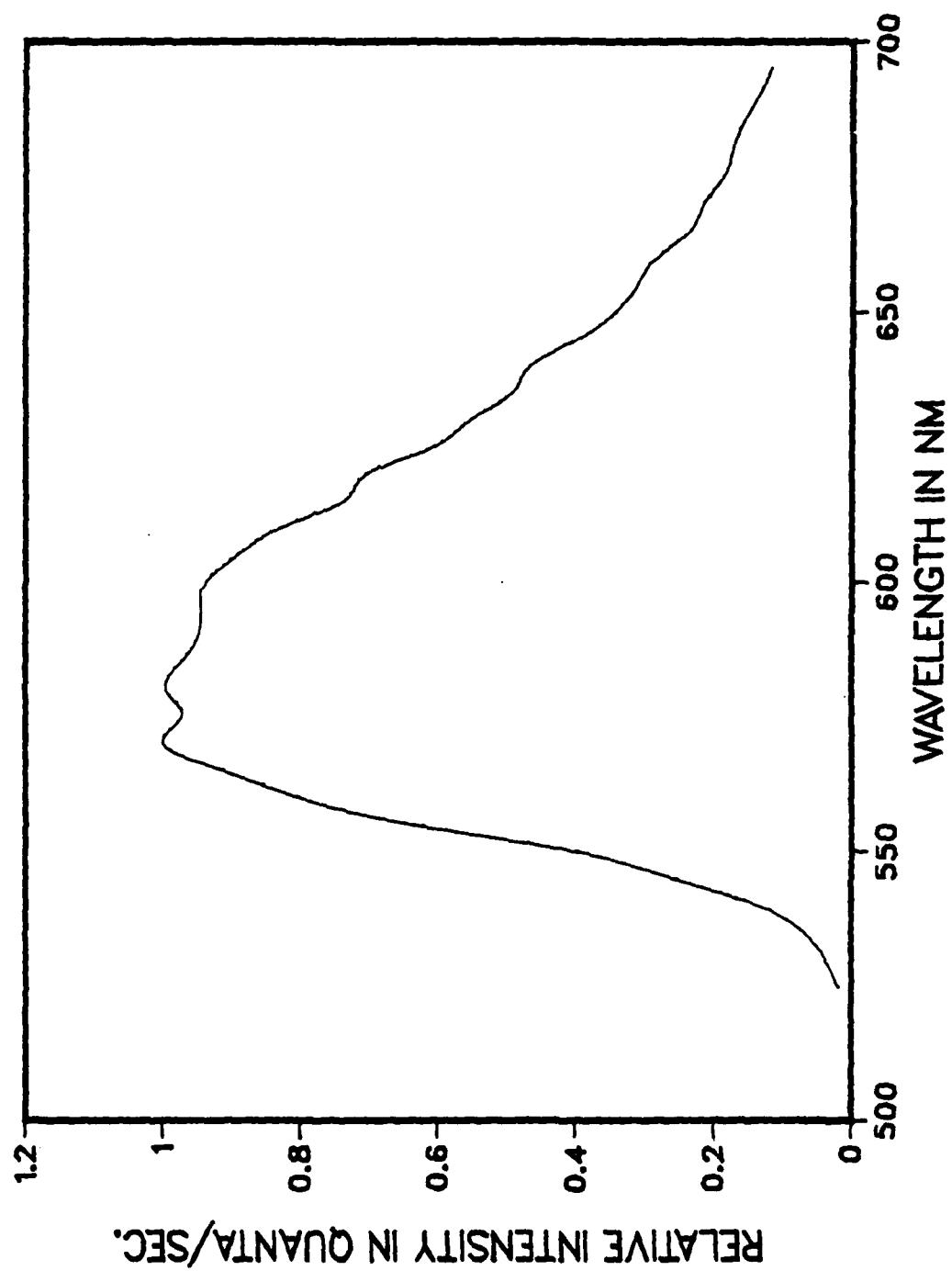


FIG.3: EFFECT OF SURFACTANT ON METQ CHEMILUMINESCENCE

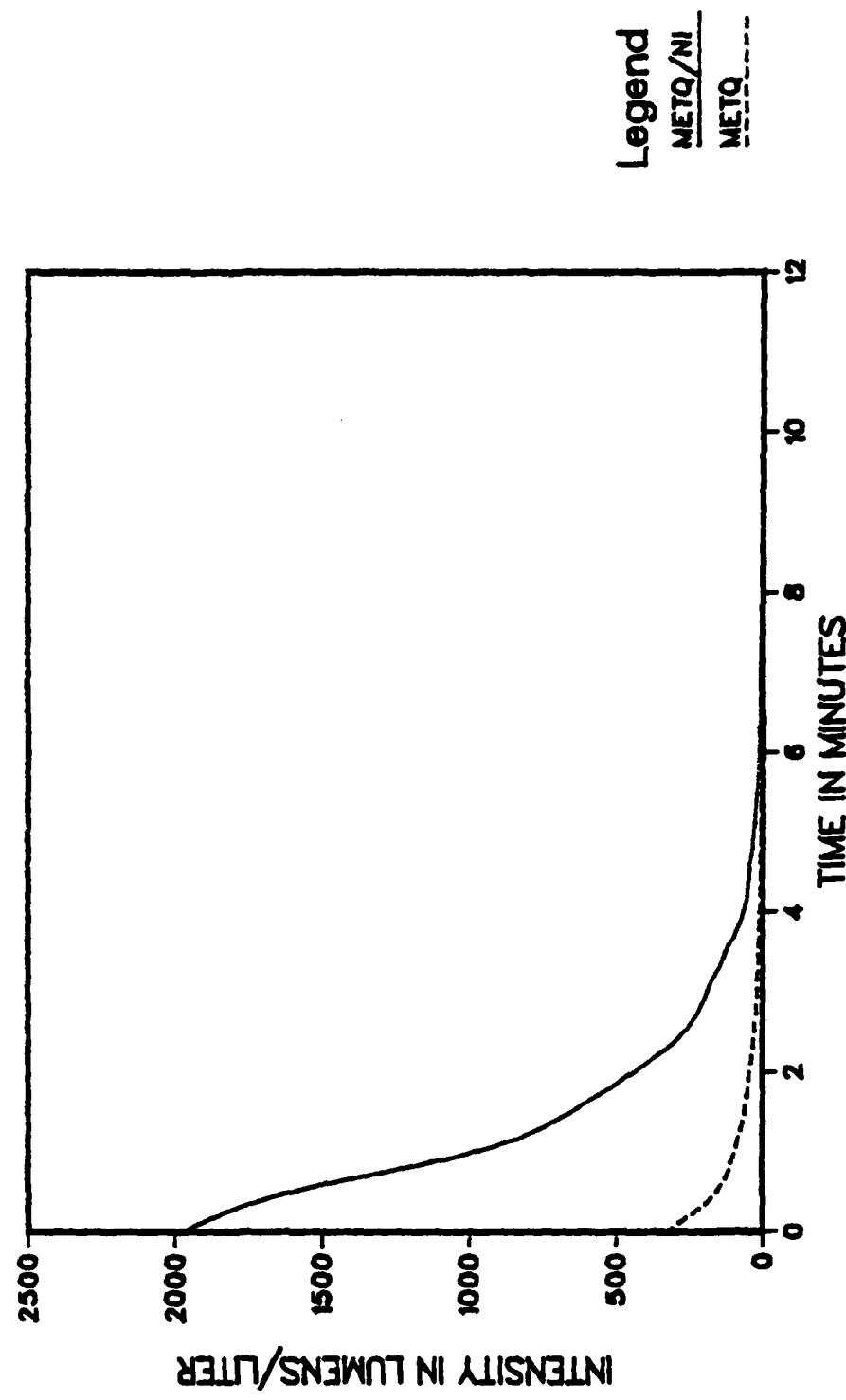


FIG.4 SPECTRAL DISTRIBUTION: PETH₁/SULFO RUBRENE

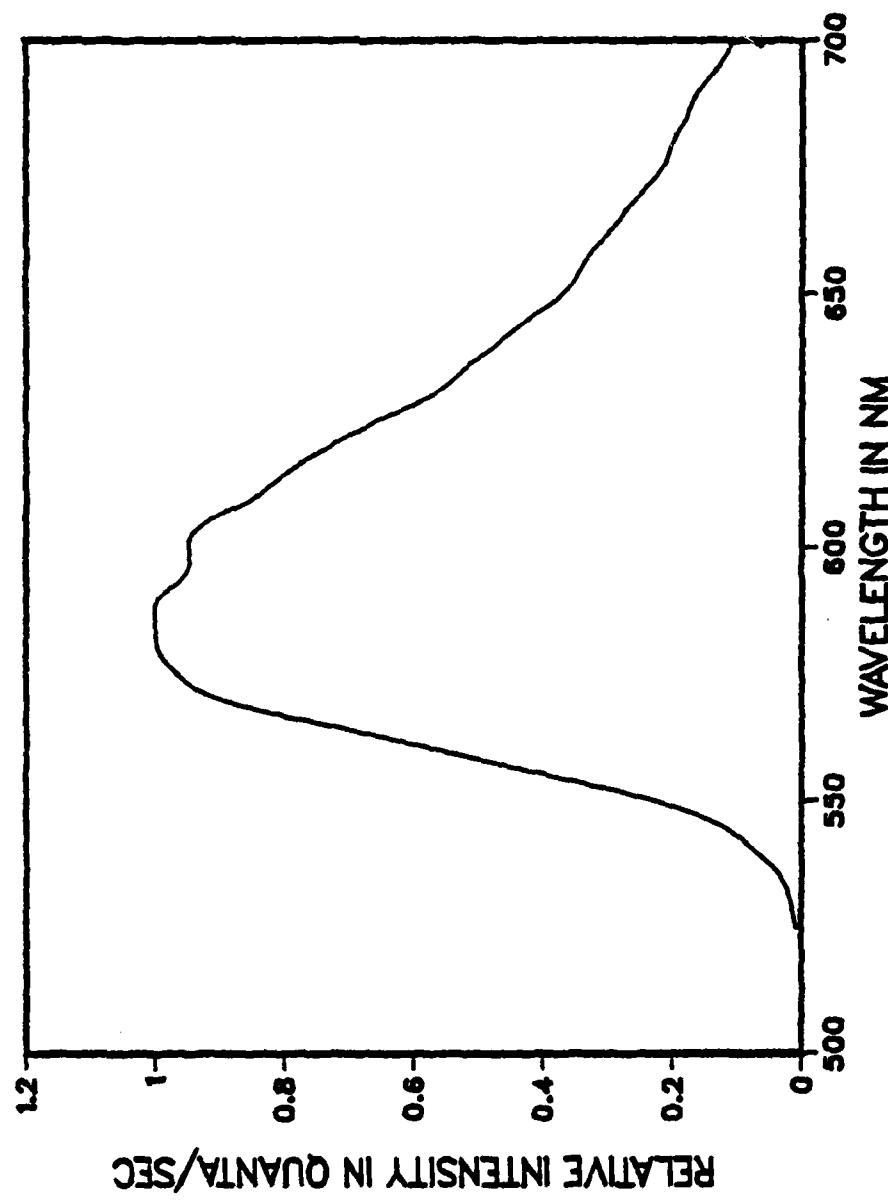


FIG.5: CHEMILUMINESCENCE OF PETH/SULFO RUBRENE

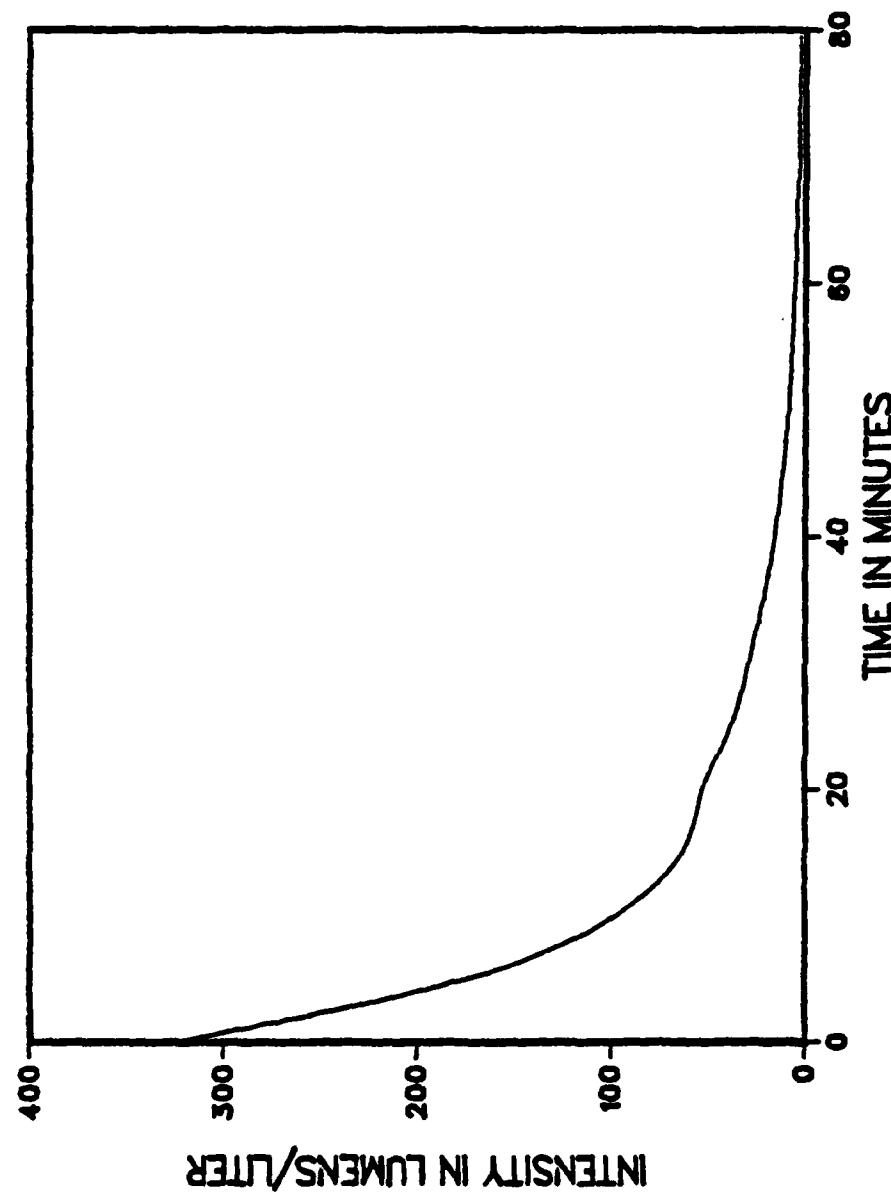


FIG.6: SPECTRAL DISTRIBUTION PETQ/RS/NI

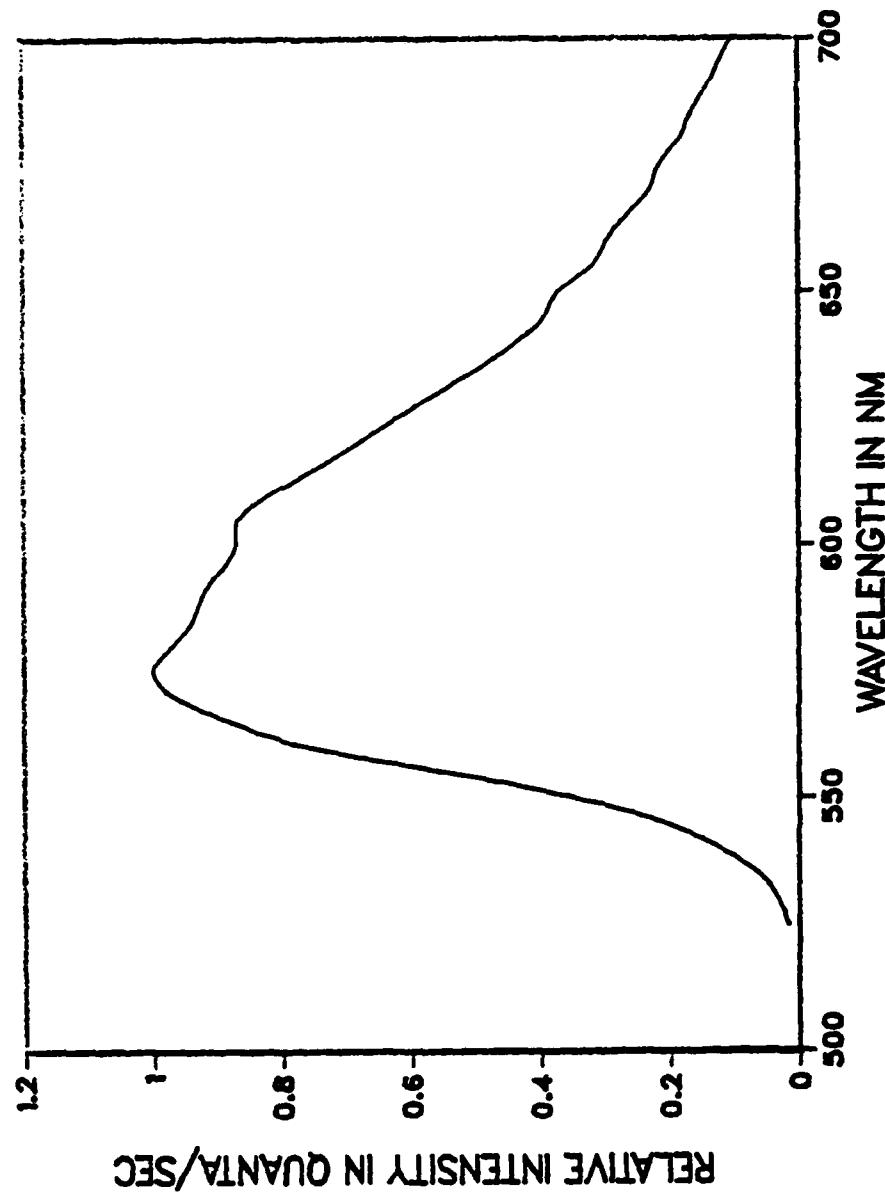
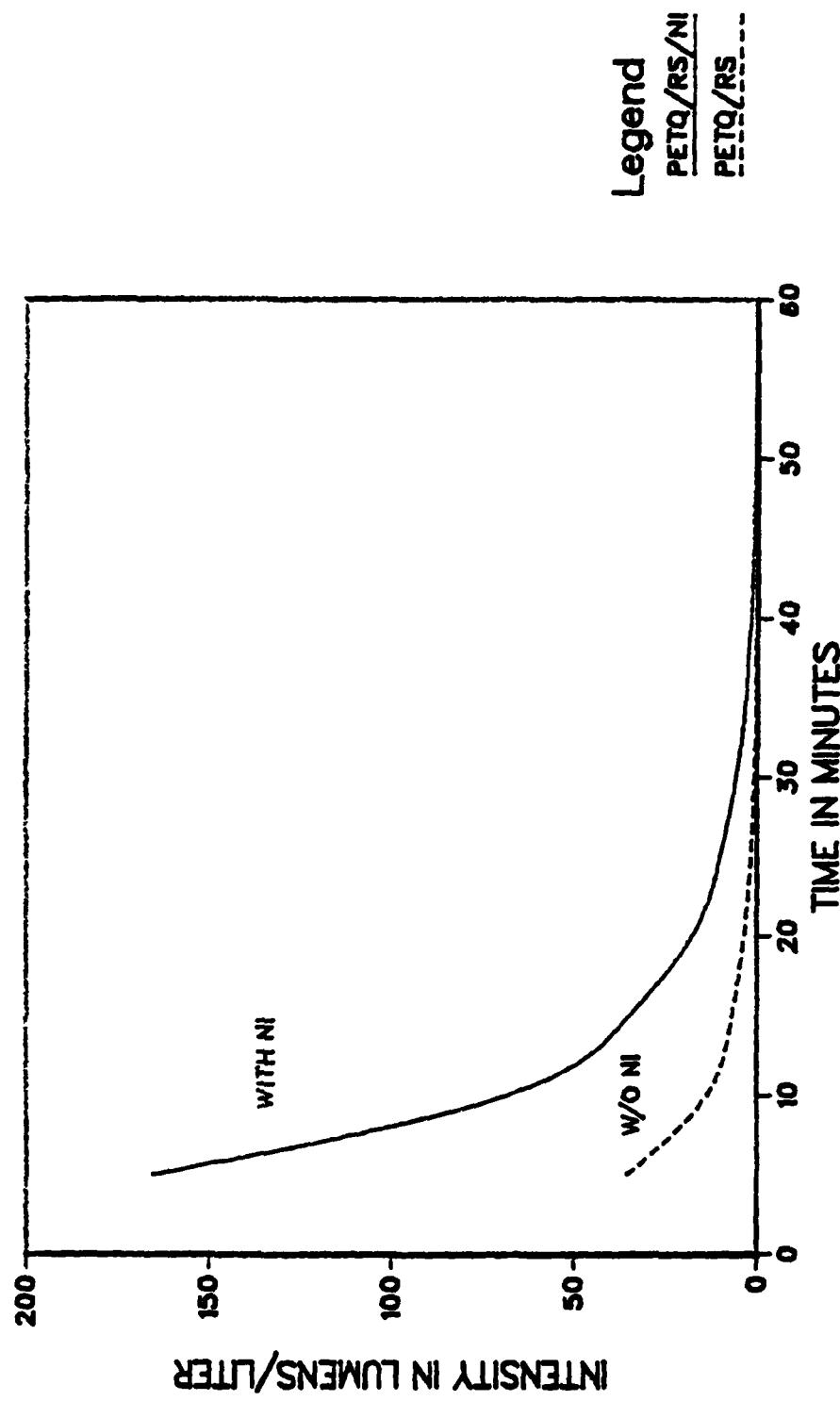


FIG.7:EFFECT OF SURFACTANT ON PETQ EFFICIENCY



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FIG.8: CHEMILUMINESCENCE OF SAPO/RS/Ni

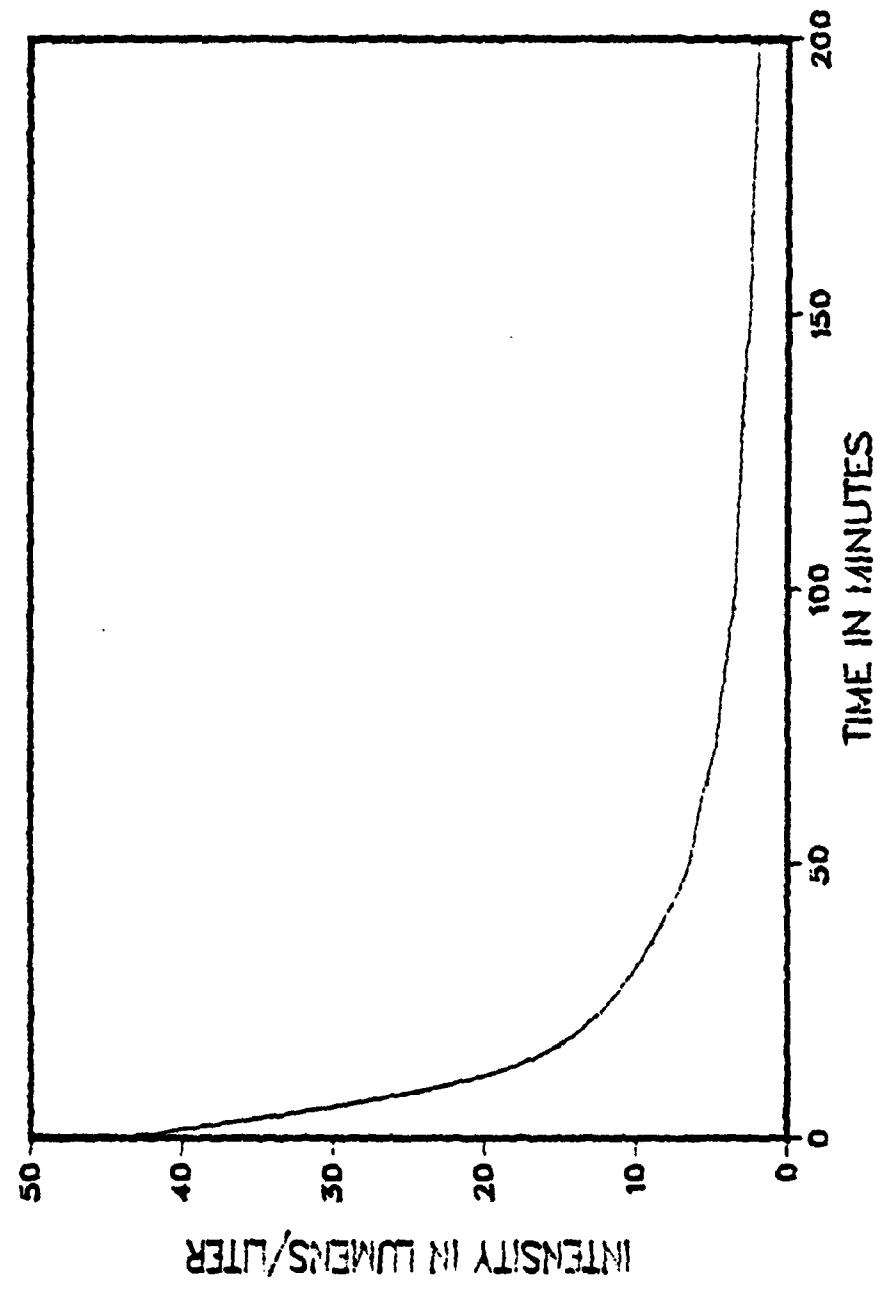


FIG.9: SPECTRAL DISTRIBUTION SAPO/RS/Ni

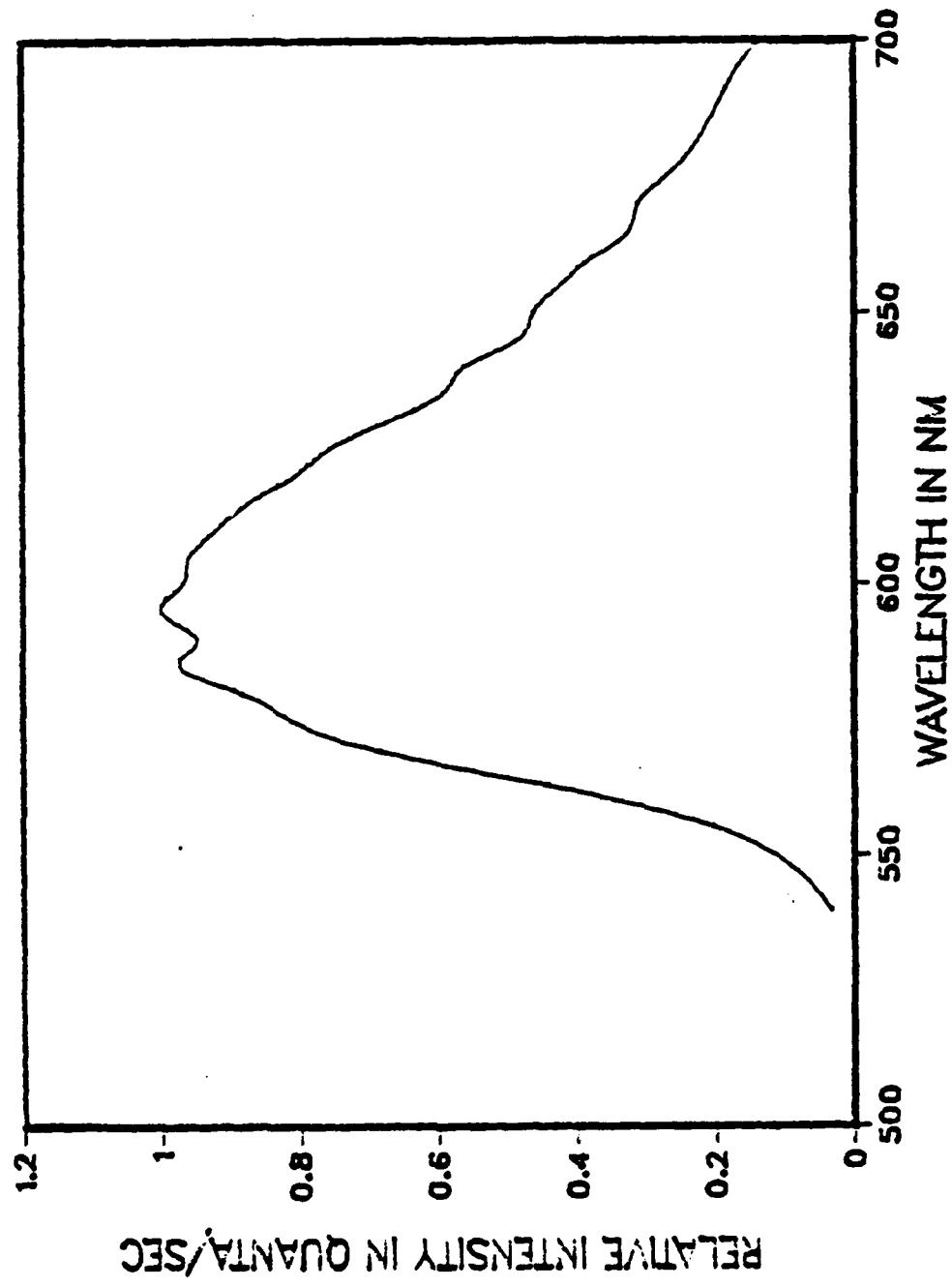


FIG. 10: SPECTRAL DISTRIBUTION: METQ/RUBRENE/CYCLOHEXANE/NI

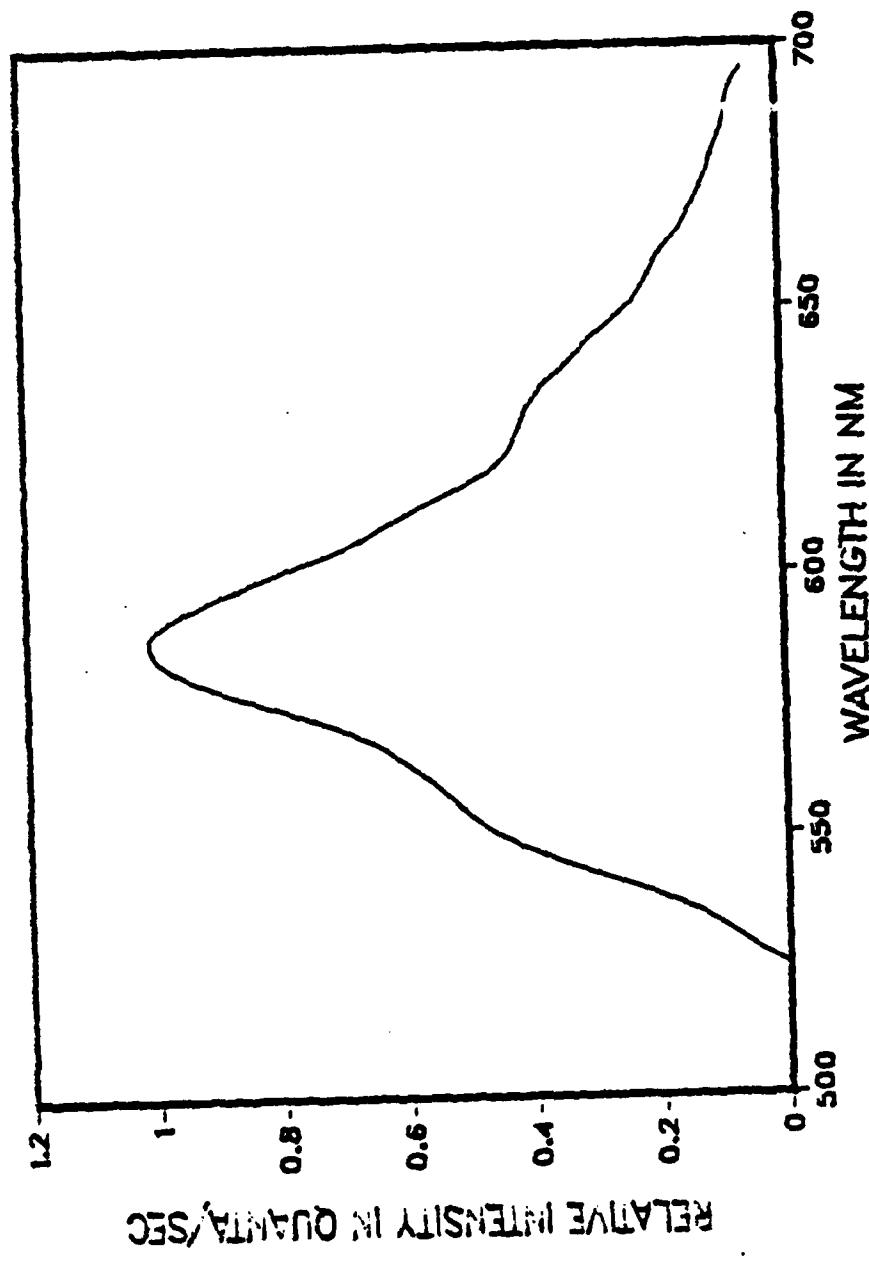


FIG.11: CHEMILUMINESCENCE OF METQ/RUBRENE/CYCLOHEXANE/NH₃

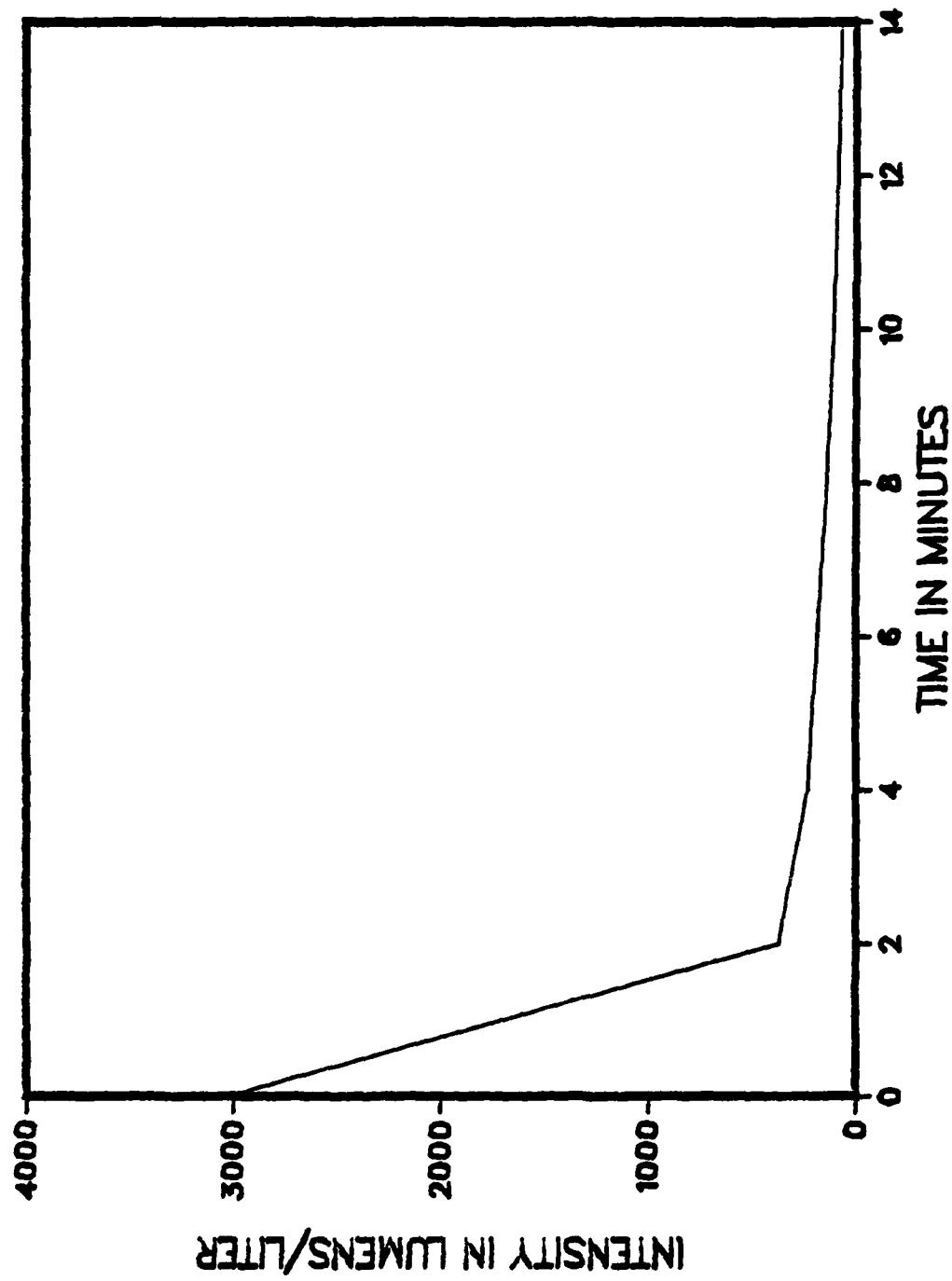


FIG.12: SPECTRAL DISTRIBUTION: BPEA AND 2-MeBPEA
IN AQUEOUS EMULSION

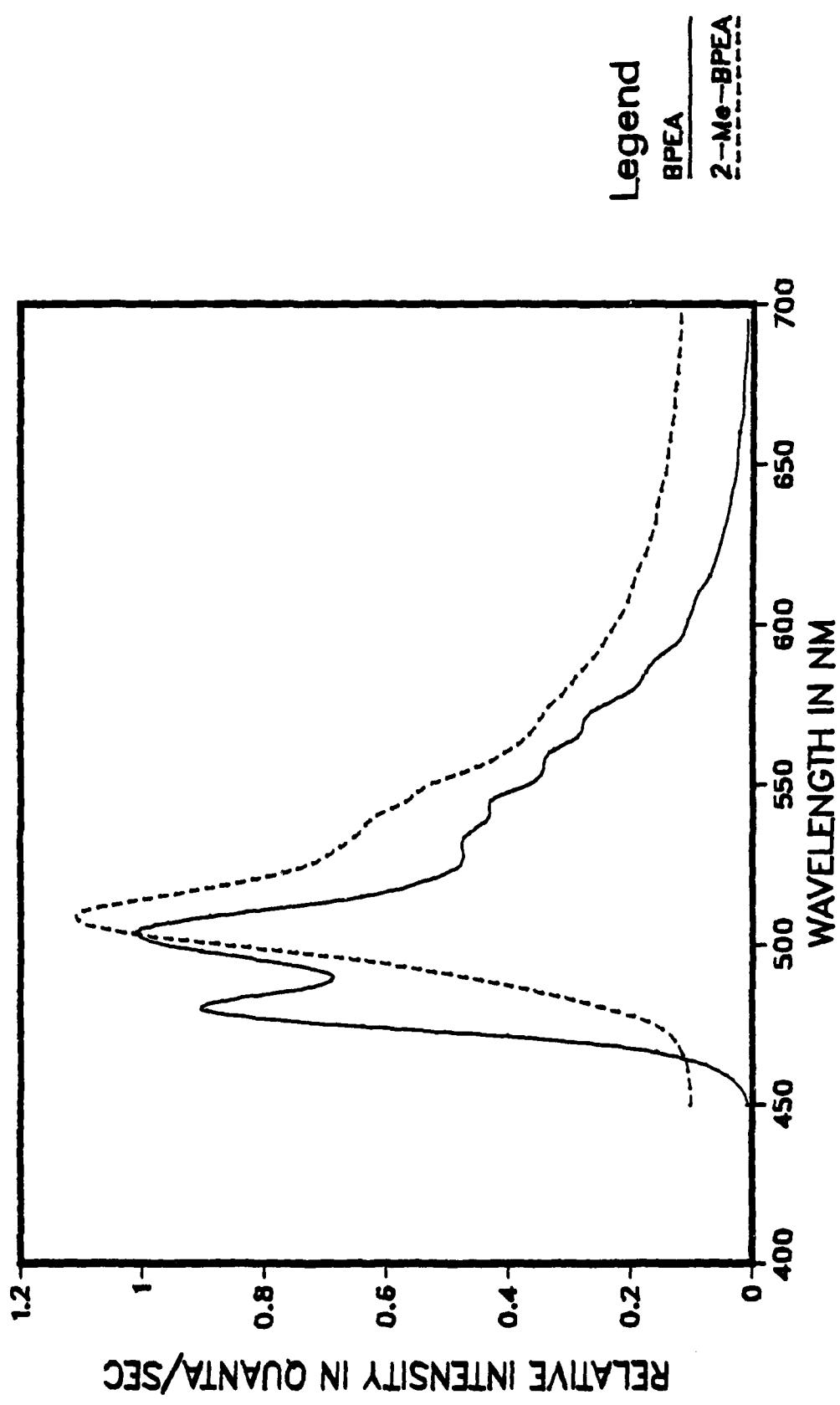


FIG.13: SPECTRAL DISTRIBUTION: BPEA AND BOBPEA
IN AQUEOUS EMULSION

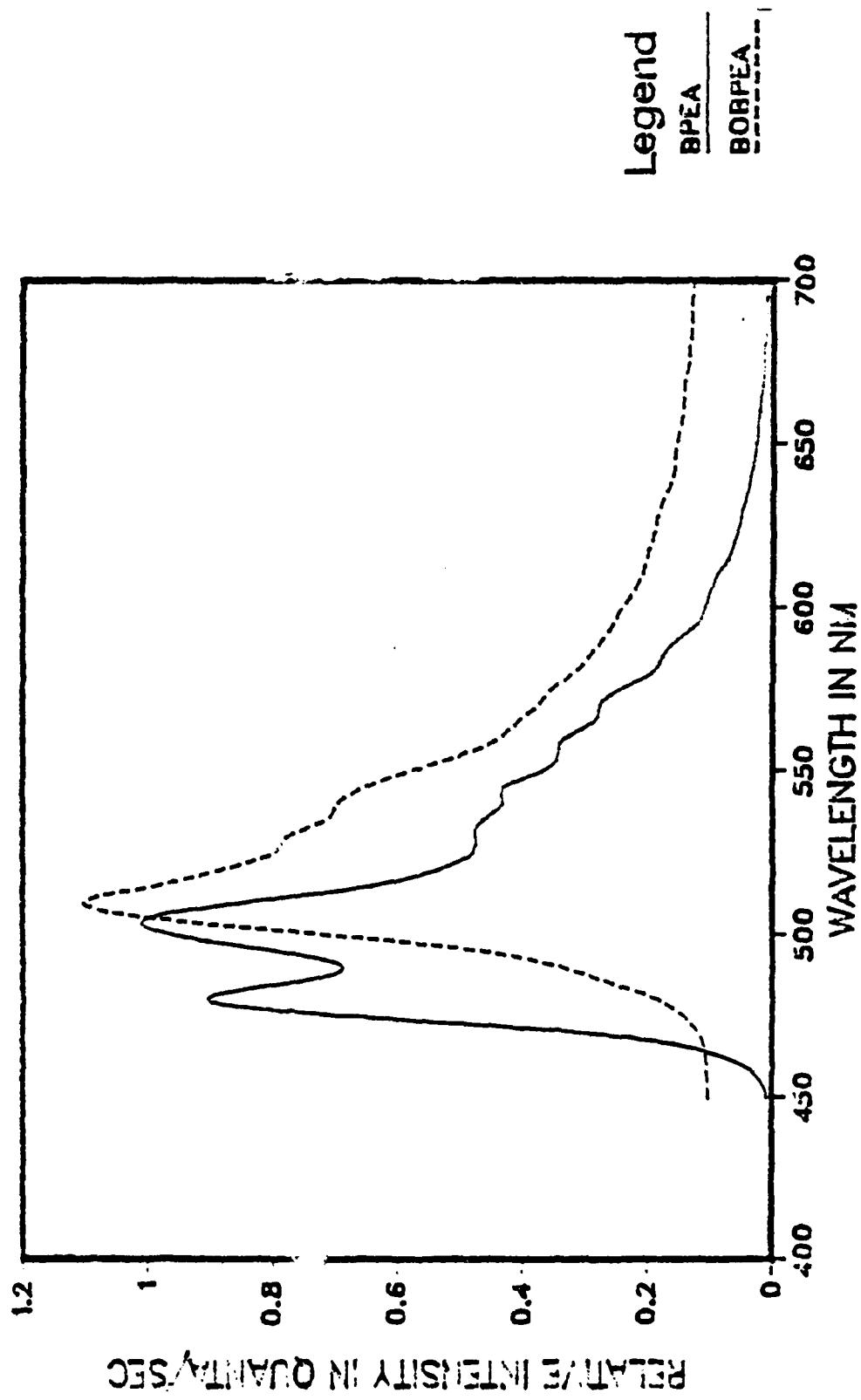


FIG. I-I: CHEMILUMINESCENCE OF ALKYL BPEA DERIVATIVES
IN AQUEOUS EMULSION

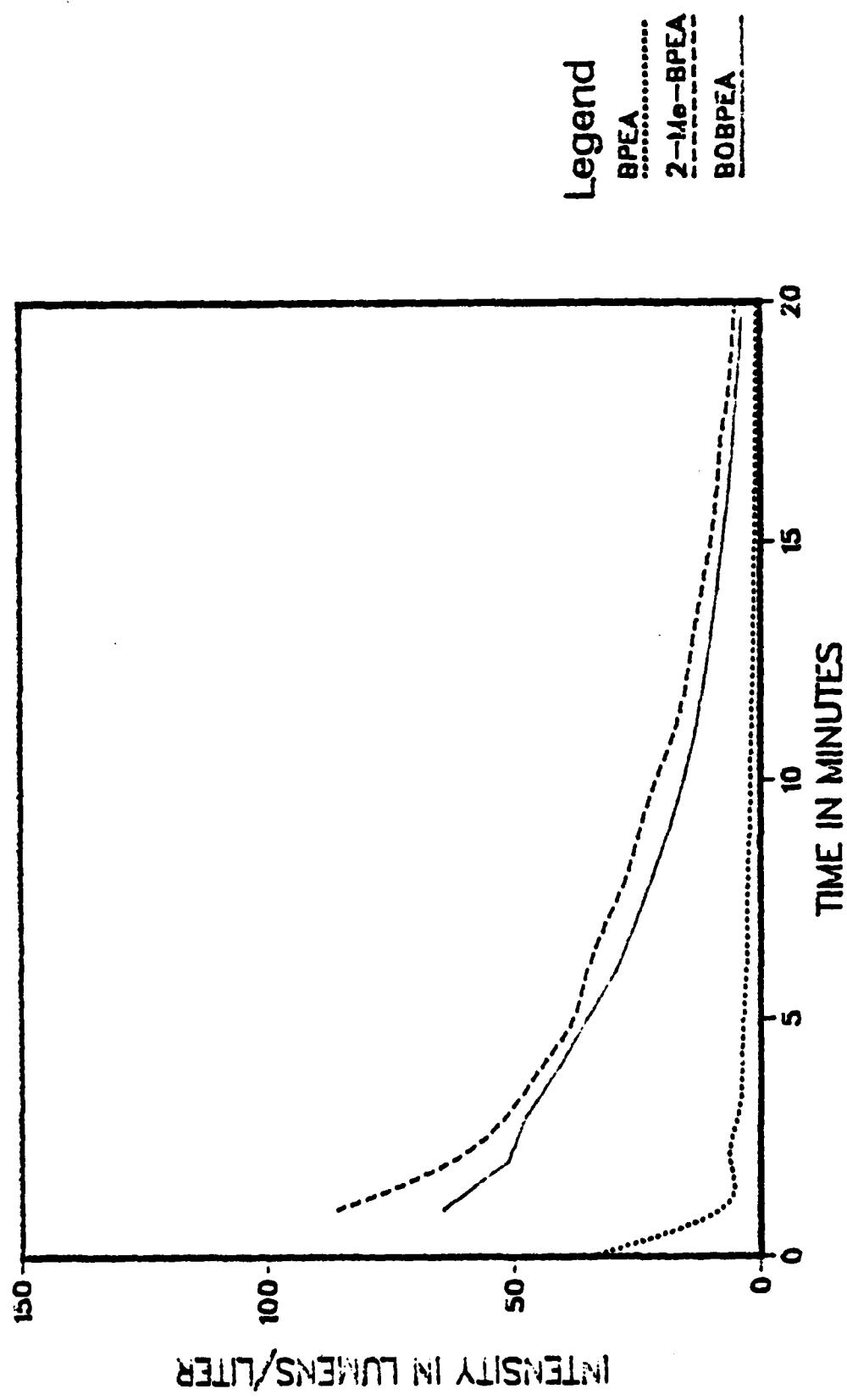
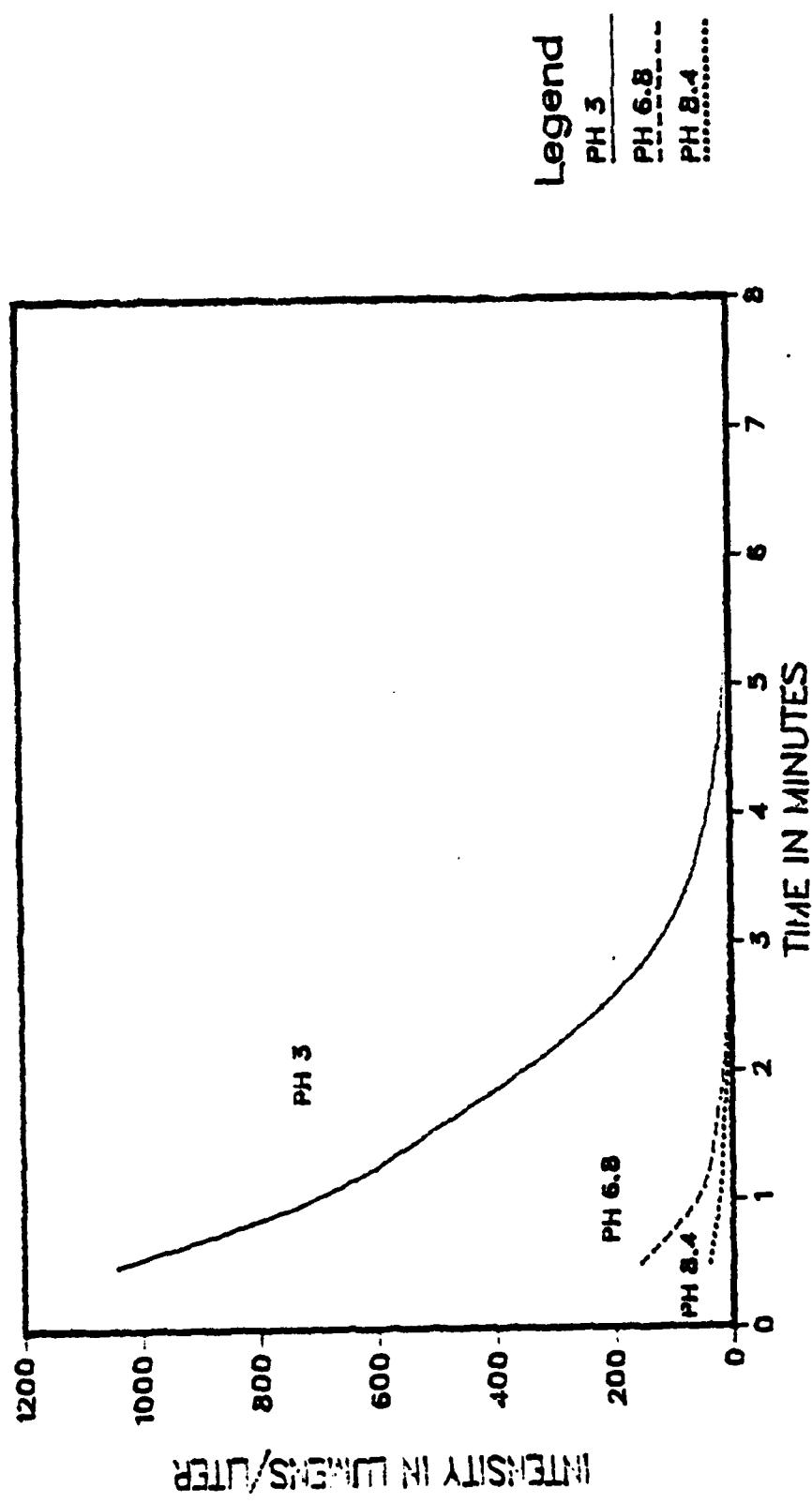


FIG.15: EFFECT OF PH ON METQ/RS/NI



Footnotes

Figures 1 - 7: Chemiluminescent reactions contained 0.04 M oxamide, 0.01 M sulforubrene, 1.75 M hydrogen peroxide, and 0.001 M "Deceresol NI" surfactant (a product of the American Cyanamid Co.) where indicated.

Figures 8 and 9: Chemiluminescent reactions contained 0.04 M SAPO, 0.01 M sulforubrene, 1.75 M hydrogen peroxide, and 0.001 M Deceresol NI surfactant.

Figures 10 and 11: Chemiluminescent reactions contained 0.04 M METQ, 0.01 M rubrene, 1.75 M hydrogen peroxide, and 0.001 M Deceresol NI surfactant in a solvent mixture of 82% water and 18% cyclohexane (by volume).

Figures 12 - 14: Chemiluminescent reactions contained 0.04 M METQ, 0.003 M of the indicated fluorescer, 1.75 M hydrogen peroxide, and 0.001 M Deceresol NI surfactant in a solvent mixture of 82% water and 18% cyclohexane (by volume).

Figure 15: Chemiluminescent reactions contained 0.04 M METQ, 0.01 M sulforubrene, 1.75 M hydrogen peroxide, and 0.001 M Deceresol NI surfactant. Solutions were buffered at the indicated pH values.

2. Non-aqueous Reactions

During the course of designing fluorescent molecules for the aqueous solvent-emulsified system, several alkyl-substituted BPEA analogs were prepared. Evaluation of these fluorescers in the non-aqueous phthalate ester solvent system gave unexpected results. Both the bis-octyl-BPEA (BOBP) and the bis-dodecyl-BPEA (BDBP) gave substantially higher quantum efficiencies than BPEA under the same conditions. Table 18 summarizes the results of these experiments.

TABLE 18: EFFECT OF ALKYL SUBSTITUTION ON EFFICIENCY OF BPEA IN PHTHALATE SOLVENT

FLR	CONC	CPPO CONC	QYx100	Lc	T.75	I _{max}
BPEA	2.25 E3 M	.08 M	12.5	279	103	1674
BOBP	"	.08	15.9	382	94	1870
BDBP	"	.08	15.4	380	101	1524
BOBP	2.25 E3	.10	12.2	366	101	2210
"	4.50 E3	.10	12.9	397	76	1895
"	6.75 E3	.10	11.6	365	110	1050
BOBP	4.50 E3	.05	14.9	230	26	2140
"	"	.05	15.5	240	26	2300
"	"	.08	13.6	340	87	2220
"	"	.10	13.7	429	88	2140
"	"	.10	13.1	414	88	2095
"	"	.15	11.6	553	168	1577
"	"	.15	11.4	540	165	1454
"	"	.20	8.37	532	151	1233
"	"	.20	8.46	532	149	1225

1. BPEA is 9,10-bis(phenylethynyl)anthracene, BOBP is 9,10-bis(p-octylphenylethynyl)anthracene, BDBP is 9,10-bis(p-dodecylphenylethynyl)anthracene.

2. Chemiluminescent reactions contained the indicated concentrations of fluorescer and CPPO along with .375 M hydrogen peroxide and 1.56 E-4 M sodium salicylate catalyst in a solvent mixture of 75% dibutyl phthalate, 20% dimethyl phthalate, and 5% t-butanol.

3. See Table 1 for heading definitions.

Typical concentration quenching is observed when the oxalate ester concentration is increased at constant BOBP concentration (see Figure 16). Variation of the fluorescer concentration at constant oxalate concentration also gives results similar to those obtained in earlier work (8) as illustrated in Figure 17. Only minor bathochromic shifts are observed in the spectral distributions from the chemiluminescent reactions (Figure 18). The shapes of the decay curves are also very similar (Figure 19). Rates of fluorescer

decomposition were measured by following the absorption maxima with time in the emitting reaction. Table 19 summarizes the results of the kinetic experiments. The kinetic data have been presented graphically in Figures 20A, 20B, 21A, and 21B.

TABLE 19: KINETICS OF THE DECOMPOSITION OF BPEA AND BOBP IN PHTHALATE SOLVENT

FLR	max	CPPO	k (1/min.) x 100
BPEA	462	.08 M	1.26
BOBP	466	.08	1.37
BPEA	438	.08	1.33
BOBP	442	.08	1.43
BPEA	462	.21	2.15
BOBP	468	.21	2.39
BPEA	438	.21	1.92
BOBP	444	.21	2.10

1. Chemiluminescent reactions contained .375 M hydrogen peroxide and 0.00016 M sodium salicylate catalyst in a solvent mixture of 75% dibutyl phthalate, 20% dimethyl phthalate, and 5% t-butanol.
2. Pseudo first-order rate constant for decomposition of the fluorescer.

3. See Table 1 for heading definitions.

Recently, it was discovered in this laboratory that N-(trifluoromethylsulfonyl)oxamides or N-triflyloxamides, which contain the most powerful known electron withdrawing group, i.e. trifluoromethylsulfonyl (triflyl), provide efficient chemiluminescent reactions in peroxyoxalate systems (6,10). A series of N-triflyloxamides (30) was prepared, and their respective chemiluminescence efficiencies in DBP were investigated. The results, summarized in Table 20, indicate that N-triflyloxamides which are further substituted on nitrogen by electronegative groups provide high chemiluminescence efficiency. Indeed, the 2,4,5-trichlorophenyl derivative proved to be the most efficient non-enzymatic chemiluminescent compound yet discovered, with a mean chemiluminescence quantum yield of 34%.

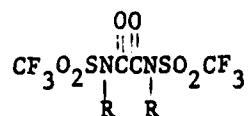


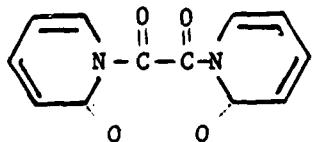
TABLE 20: CHEMILUMINESCENCE PERFORMANCE OF N-TRIFLYLOXAMIDES, 30, IN NON-AQUEOUS MEDIA

Compound <u>30</u>	QYx100	Lc
<u>R</u> =		
4-chlorophenyl	11.4	37.5
2,4-dichlorophenyl	26.2 , 25.6	85.0 , 85.4
2,4,5-trichlorophenyl	32.6 , 35.4	108 , 117
2,4,6-trichlorophenyl	11.4 , 13.6	37.8 , 45.0
4-nitrophenyl	11.0	35.7
ethyl	2.59	8.4
ethyl	4.47	15.0
2-methoxyethyl	2.85	9.2
2-chloroethyl	3.68	12.2
trifluoroethyl	12.7	41
morpholinoethyl (<u>31</u>)	nil	
pyridylethyl	.069	.23
cyclopropyl	3.39	11.4
3-chloropropyl	1.48	5.0
allyl	2.44	8.2
carbethoxymethyl (<u>32</u>)	12.8	42
carbobenzylloxymethyl (<u>33</u>)	10.0	32.5
2-chloro-3-pyridyl (<u>34</u>)	15.5	41.3

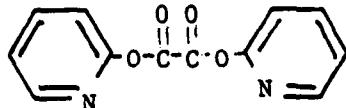
1. Chemiluminescent reactions contained .00675 M 1-chloro-9,10-bis(phenylethynyl)anthracene, .375 M hydrogen peroxide, .0003 M sodium salicylate and .01 M oxamide in a solvent mixture of 75% (by volume) dibutyl phthalate, 20% dimethyl phthalate and 5% t-butanol.

2. See Table 1 for heading definitions.

It was shown in an earlier study (13) that the reaction of oxalyl chloride with 2-hydroxypyridine yielded the oxamide, 35, rather than the expected oxalate ester, 36. Chemiluminescence was observed from the reaction of 35 with acid catalysis. Apparently the product was derived from tautomerization of 2-hydroxypyridine in the presence of oxalyl chloride. The possibility of tautomerization does not exist with 3-hydroxypyridine so that treatment of this isomer with oxalyl chloride in the presence of triethylamine gives the expected ester, 37. The oxalate ester 37 gave a strong but short-lived chemiluminescent reaction in the phthalate solvent system.

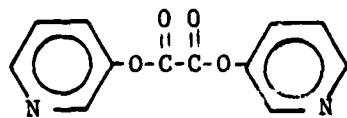
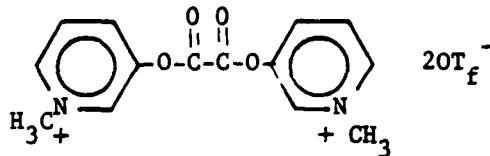


35



36

Quaternization of 37 afforded the bis-quaternary ammonium salt, 38, which gave substantial chemiluminescence in dibutyl phthalate but was not chemiluminescent in water. Infrared and NMR studies indicated that 38 underwent rapid hydrolysis in water within 5 minutes of mixing. A number of other pyridyl and quinolyl oxalate esters were prepared, and their performance in dibutyl phthalate is summarized in Table 21.

3738

$$T_f = SO_2CF_3$$

TABLE 21: CHEMILUMINESCENCE PERFORMANCE OF PYRIDYL AND QUINOLYL OXALATE ESTERS IN DIBUTYL PHTHALATE

Oxalate ester	Conc.	QYx100	T.75	Lc
<u>37</u>	.01 M	.054	.30	.16
<u>39</u>	.01	.277	1.5	.90
<u>40</u>	.01	1.58	1.4	5.23
<u>41</u>	.001	.147		.05
<u>42</u>	.001	.033	.22	.01
<u>43</u>	.001	2.68	35	8.97

1. Chemiluminescent reactions contained the indicated concentrations of the oxalate ester, .00675 M 1-chloro-9,10-bis(phenylethynyl)-anthracene, .375 M hydrogen peroxide, and .0003 M sodium salicylate in a solvent mixture of 75% (by volume) dibutyl phthalate, 20% dimethyl phthalate and 5% t-butanol.

2. See Table 1 for heading definitions.

Oxalate Esters in Table 21

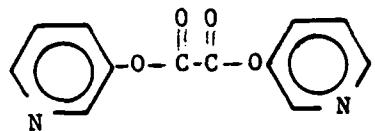
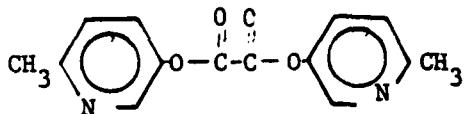
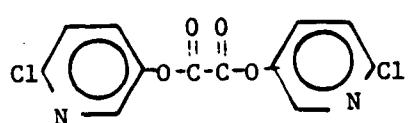
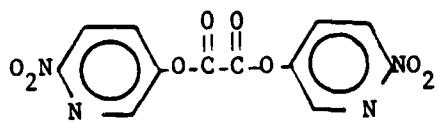
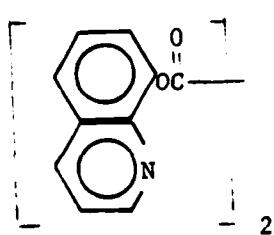
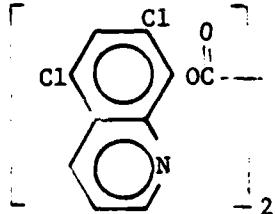
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FIG.16: EFFECT OF CPPO CONCENTRATION
ON BOBPEA EFFICIENCY

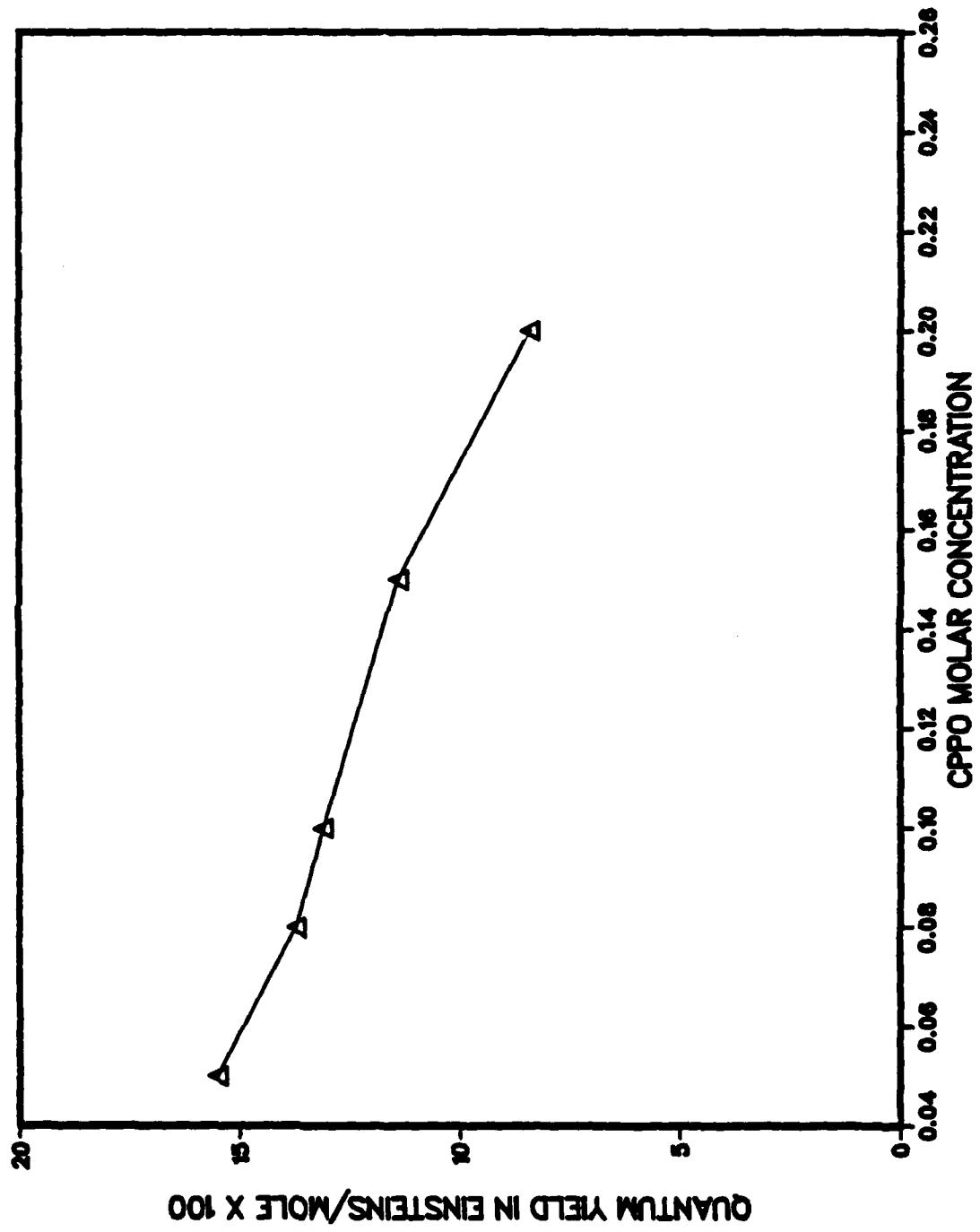


FIG.17: EFFECT OF BOBPEA CONCENTRATION
ON BOBPEA EFFICIENCY

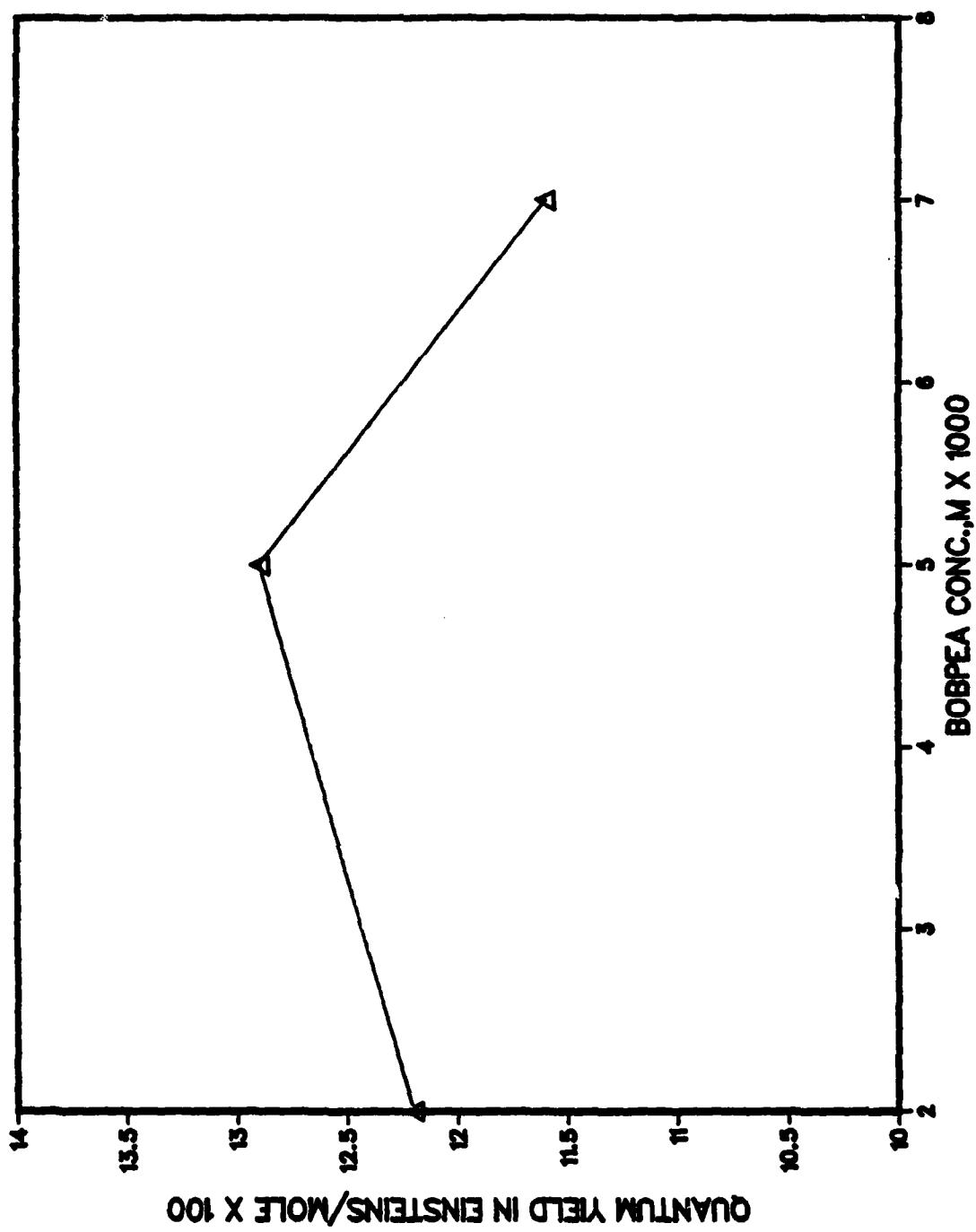


FIG.18: SPECTRAL DISTRIBUTION OF BPEA, BOBPEA and BDDBPEA
IN PHthalate SOLVENT

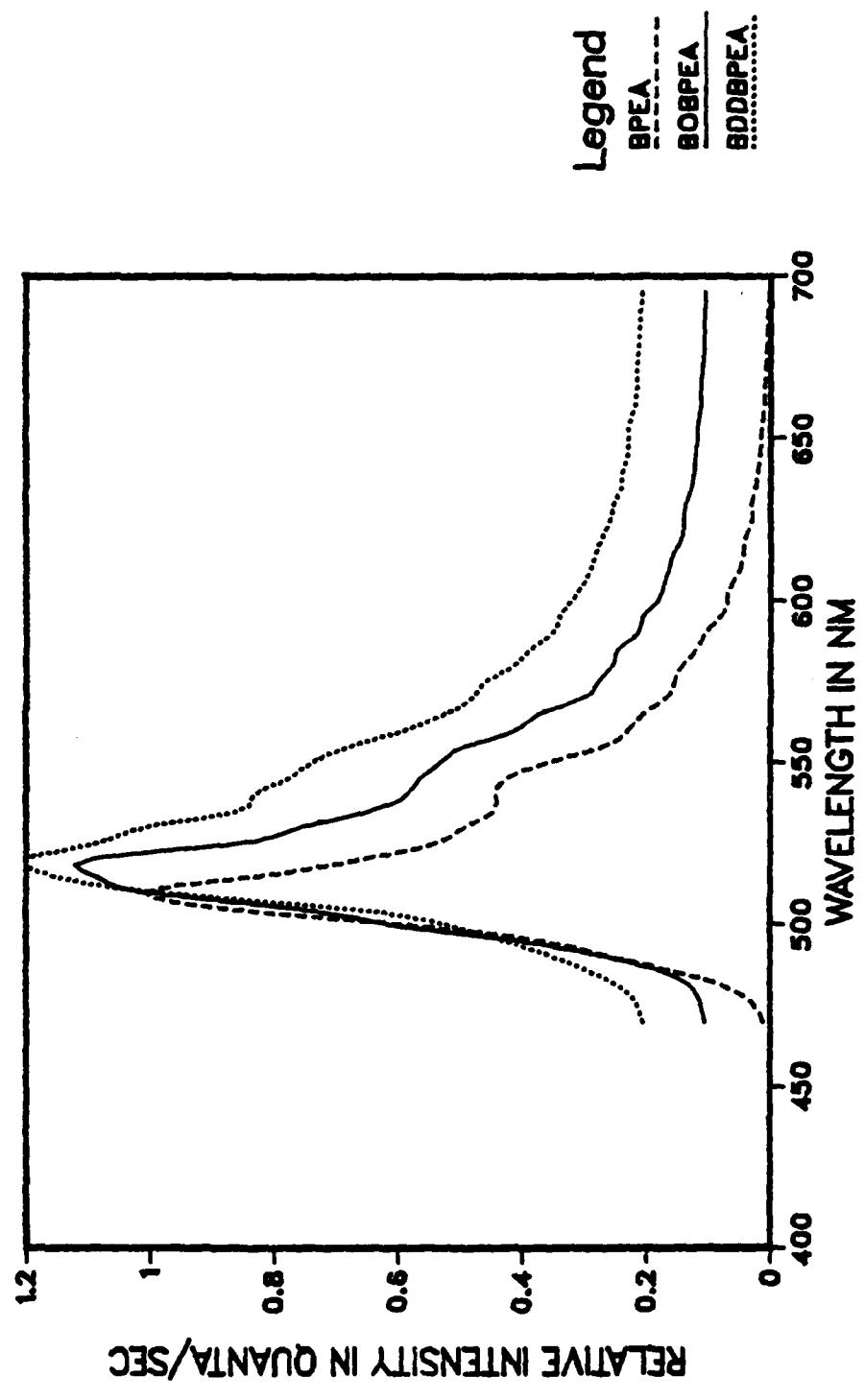


FIG.19: CHEMILUMINESCENCE OF BPEA, BOBPPEA and BDDDBPEA
IN PHthalate SOLVENT

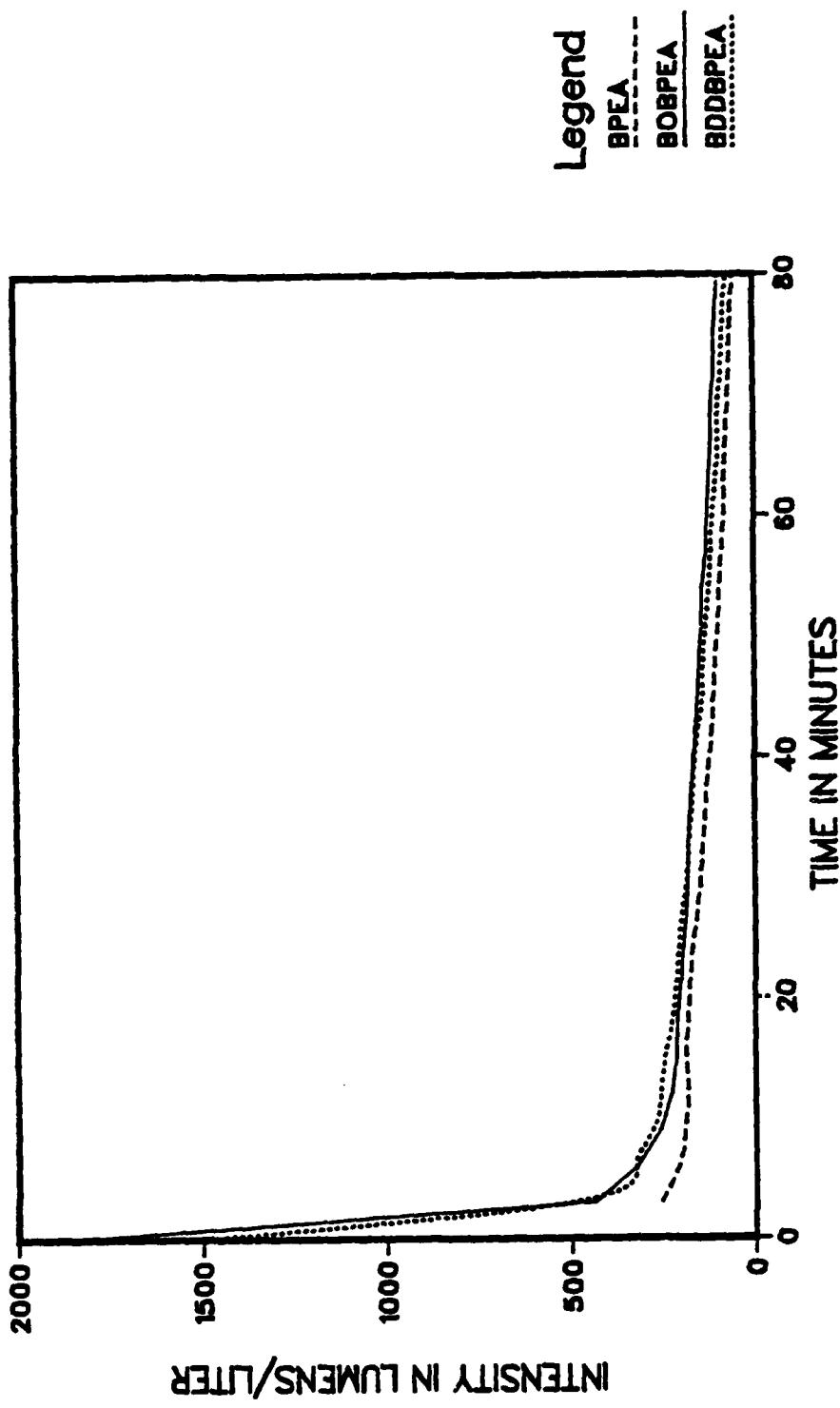


FIG.20A: DECOMPOSITION OF BPEA AND BOBPEA

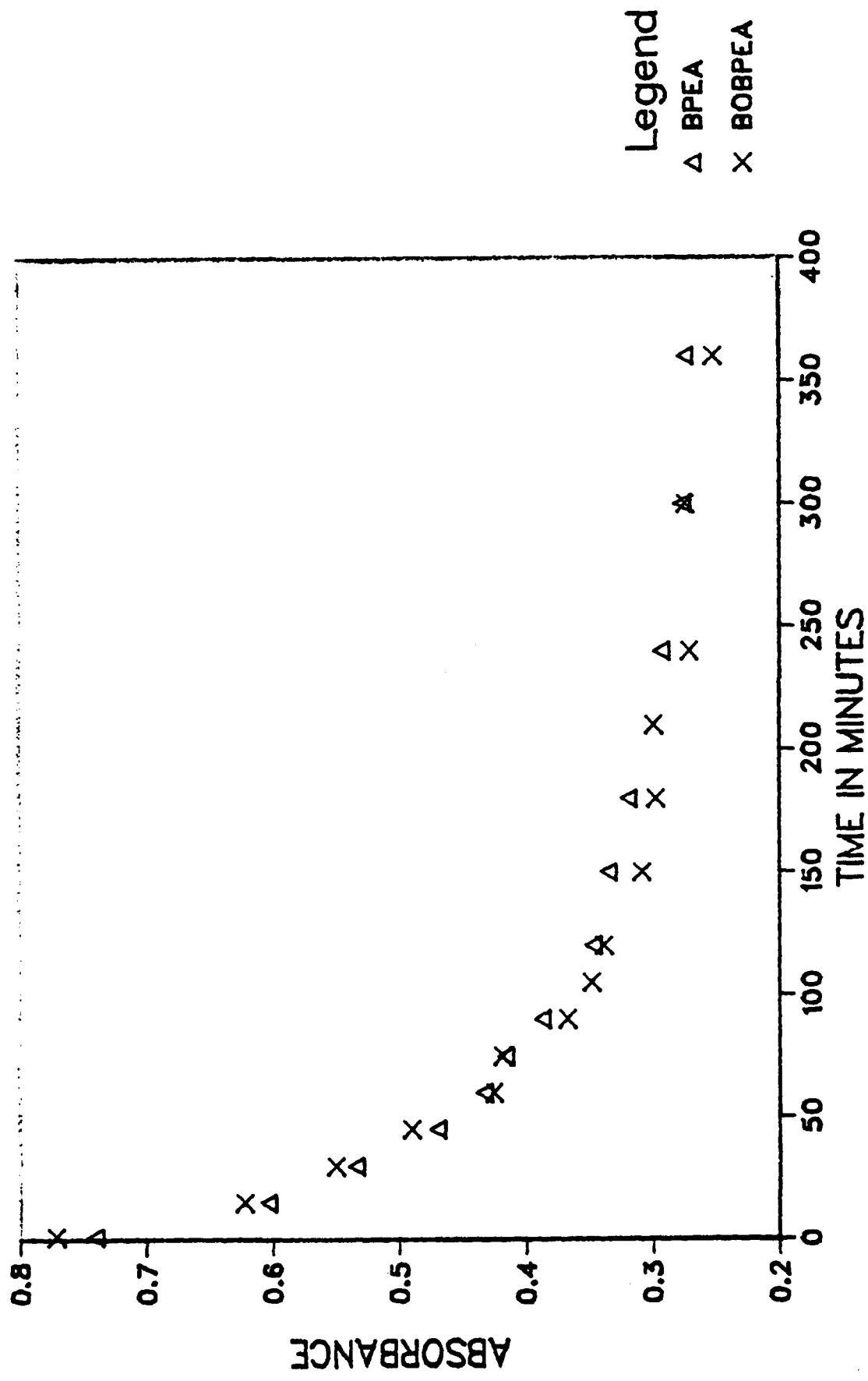


FIG.20B:DECOMPOSITION OF BPEA AND BOBPEA
PSEUDO FIRST-ORDER KINETICS

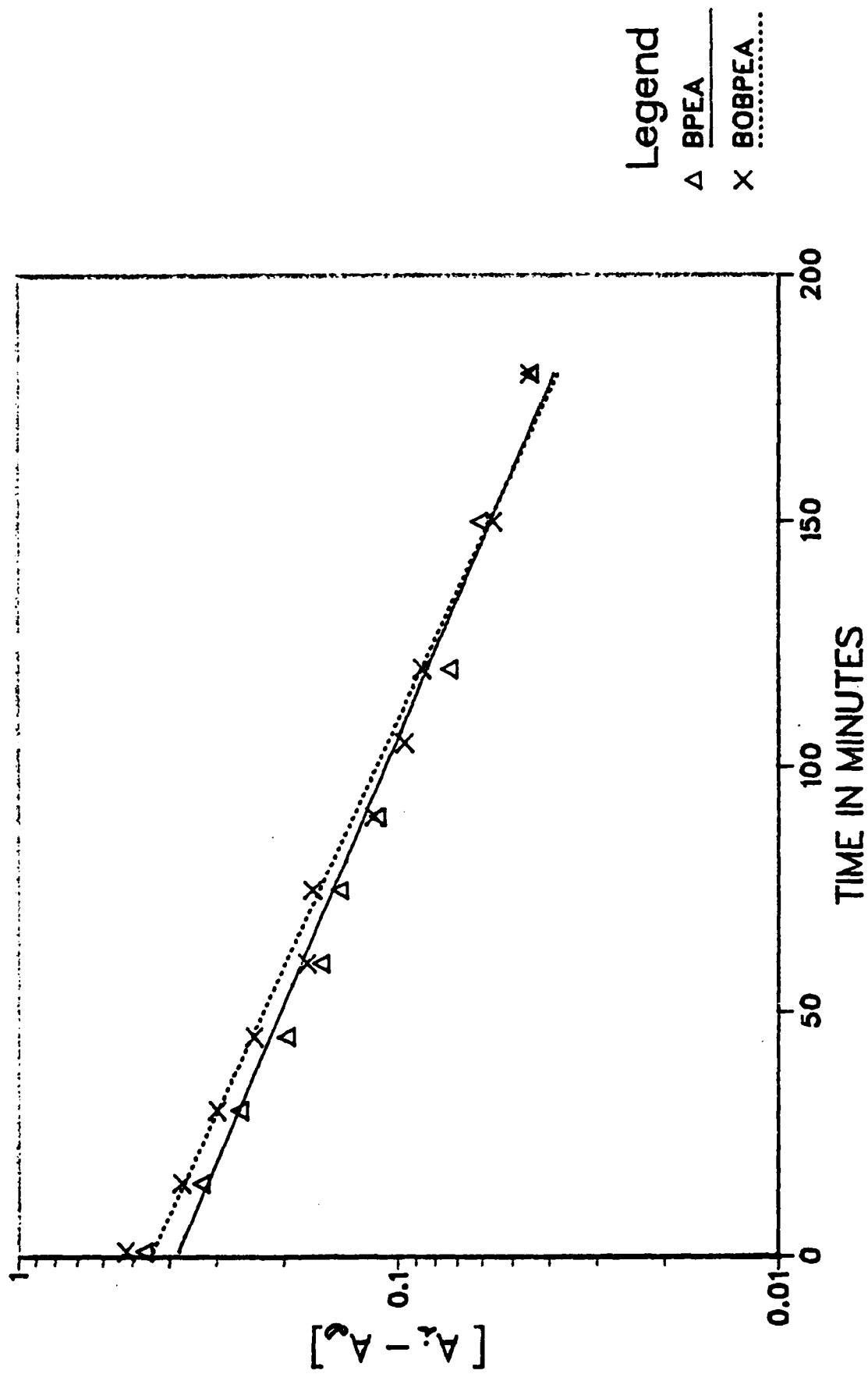


FIG.21A: DECOMPOSITION OF BPEA AND BOBPEA

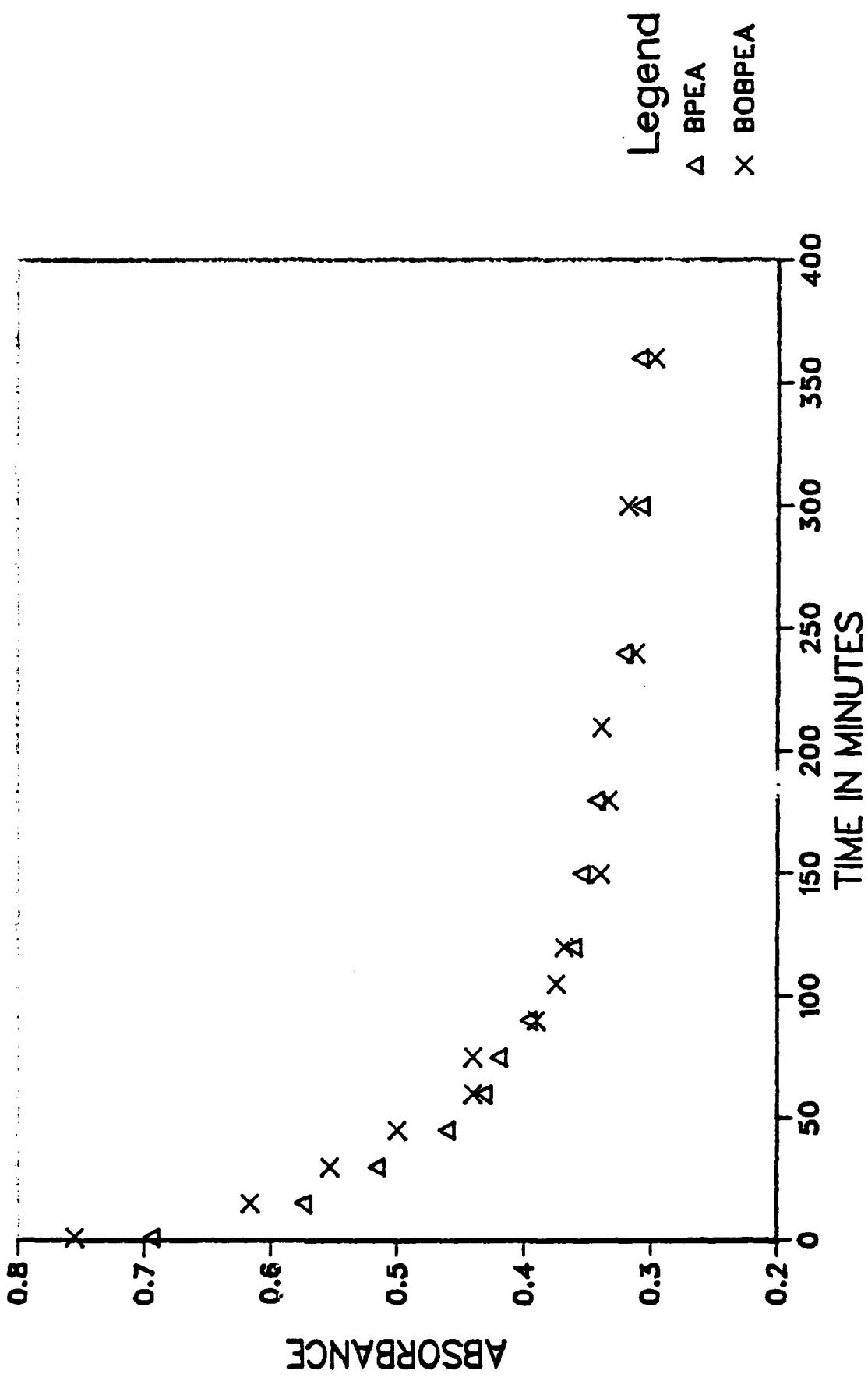
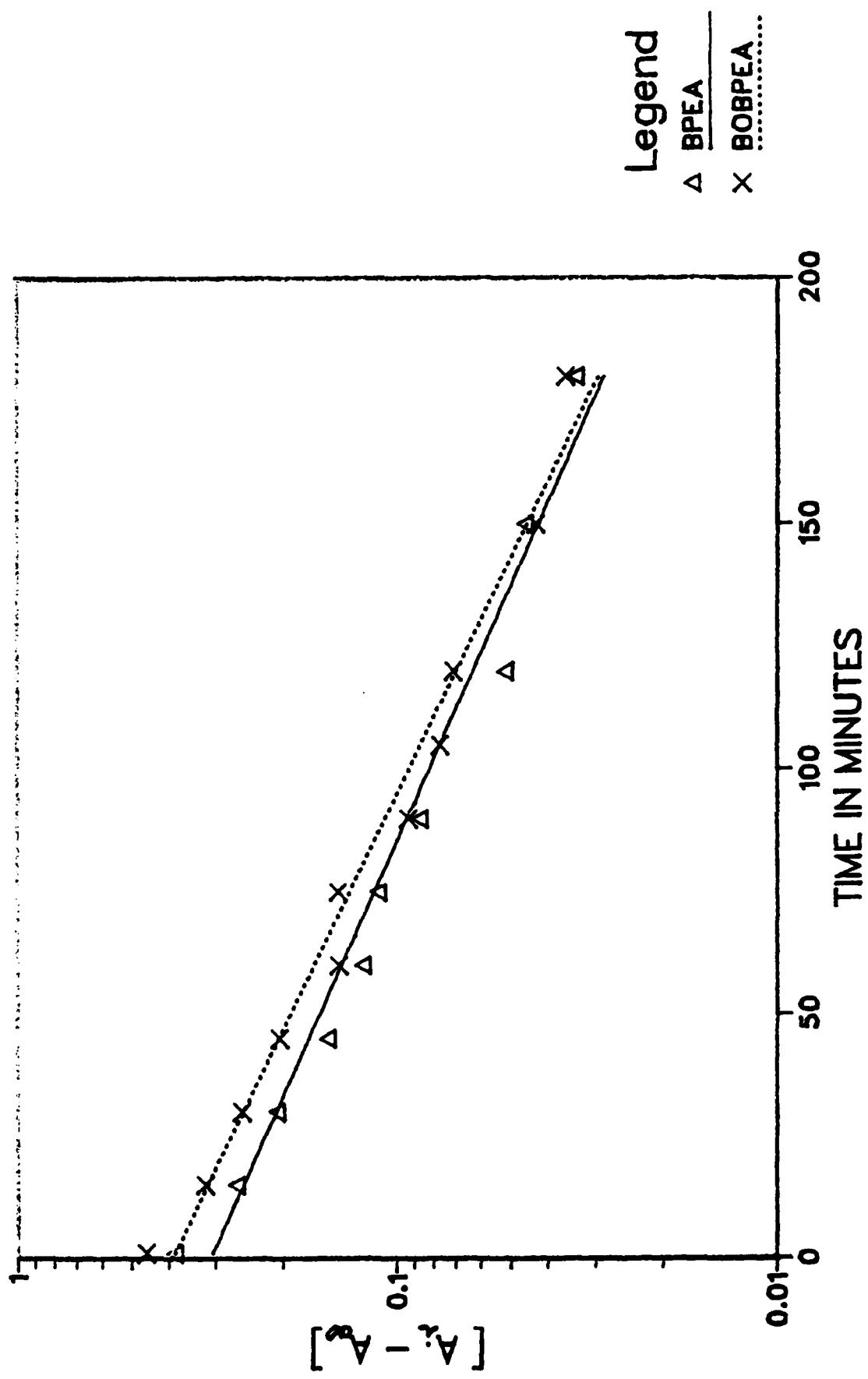


FIG. 21B: DECOMPOSITION OF BPEA AND BOBPEA
PSEUDO FIRST-ORDER KINETICS



Footnotes

Figure 16: Chemiluminescent reactions contained 0.0045 M BOBP, the indicated amount of CPPO, 0.375 M hydrogen peroxide, and 0.00016 M sodium salicylate catalyst in a solvent mixture of 75% dibutyl phthalate, 20% dimethyl phthalate, and 5% t-butanol.

Figure 17: Chemiluminescent reactions contained the indicated amount of BOBP, 0.10 M CPPO, 0.375 M hydrogen peroxide, and 0.00016 M sodium salicylate catalyst in a solvent mixture of 75% dibutyl phthalate, 20% dimethyl phthalate, and 5% t-butanol.

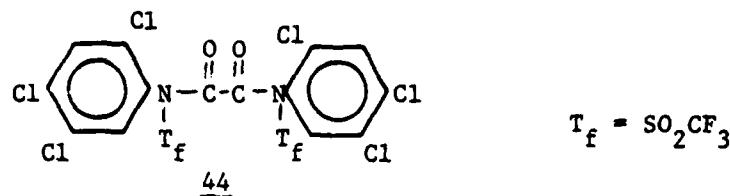
Figures 18 and 19: Chemiluminescent reactions contained 0.00225 M fluorescer, 0.08 M CPPO, 0.375 M hydrogen peroxide, and 0.00016 M sodium salicylate catalyst in a solvent mixture of 75% dibutyl phthalate, 20% dimethyl phthalate, and 5% t-butanol.

Figures 20A, 20B, 21A, and 21B: Kinetic experiments were carried out with 0.00225 M fluorescer, CPPO concentrations of 0.08 M (Figures 20A and 20B) and 0.21 M (Figures 21A and 21B), 0.375 M hydrogen peroxide, and 0.00016 M sodium salicylate catalyst in a solvent mixture of 75% dibutyl phthalate, 20% dimethyl phthalate, and 5% t-butanol. Aliquots were removed from the reaction and diluted 1/100 with dibutyl phthalate and analyzed on the spectrophotometer. Reactions were run in a thermostatted bath at 25 C.

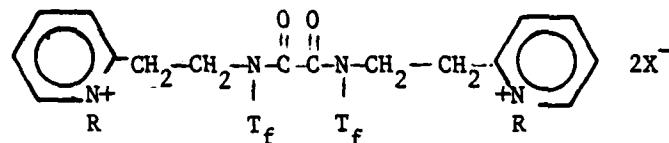
B. DISCUSSION

1. Aqueous Reactions

A series of water soluble triflyl oxamides was prepared in an effort to exploit the high efficiency found for bis(2,4,5-trichlorophenyl)triflyloxamide, 44, in chemiluminescent reactions carried out in organic solvents.

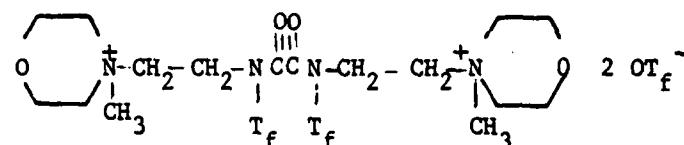


The performance of PETQ (1), PETH (2) and METQ (4) was measured in the aqueous chemiluminescent reaction (see Tables 1 and 2).



1 PETQ: $\text{R} = \text{CH}_3$, $\text{X} = \text{OT}_f$

2 PETH: $\text{R} = \text{H}$, $\text{X} = \text{Cl}$



3 METQ

The oxamide PETQ gave a chemiluminescent quantum yield of 1.45% in water using sulfonated rubrene as the fluorescer. METQ was somewhat less efficient with a quantum yield of 0.64%. The addition of the nonionic surfactant, "Deceresol NI", gave four to seven-fold

increases in efficiency depending on the structure of the oxamide. The rate of light decay follow pseudo-first order kinetics with the METQ rate over four times faster than the PETQ rate. It was interesting that no difference in the light decay rate was found in the presence or absence of the surfactant. Spectral measurements indicated no significant change in the spectral distribution of the chemiluminescent reactions in the presence of the nonionic surfactant.

The enhancement of chemiluminescent efficiency in the presence of the nonionic surfactant appeared to be a general phenomenon, not restricted to oxamides. Improvement was also found with oxalic esters (see Tables 3, 4 and 5). It is interesting that the first oxalic ester to show any significant activity in water, SAPO, gave an improvement of over 1000 times with the combination of sulforubrene and surfactant compared to the original result with the sulfonated pyrene derivative HPTS.

The structure of the fluorescer is vitally important in obtaining highly efficient peroxyoxalate chemiluminescent reactions. It appears that it is even more critical in aqueous systems than in organic solvents. Rubrene is known (4) to be one of the most efficient fluorescers in non-aqueous reactions, but undergoes rapid photoxidation under the reaction conditions particularly at higher concentrations of the oxalic ester. It is known (14) that incorporation of a readily photo-oxidized hydrocarbon into a micelle substantially retards the rate of photo-oxidation, thus one function of the surfactant may be protection of the fluorescer during the aqueous reaction. Substitution of cationic, nonionic or anionic water-solubilizing groups onto the rubrene nucleus gave efficient aqueous chemiluminescent reactions (Table 6), but similar substitutions in the phenylethynyl anthracene series gave substantially lower quantum yields (Table 7). Analogous results were found in a series of water soluble pyrene derivatives (Table 8).

As evidenced by the syntheses described in Section IV below, the design, synthesis and particularly purification of water-soluble fluorescers is difficult. One approach to an aqueous chemiluminescent system is to emulsify the fluorescer in an organic solvent and react the water-soluble oxalic acid derivative with hydrogen peroxide in the aqueous phase. The key intermediate could then, in principle, migrate into the organic phase, excite the fluorescer, and produce light. This avoids the requirement that the fluorescer be soluble in water and greatly simplifies the synthesis. This approach was successful (see Table 9) with rubrene and several substituted rubrenes. The efficiencies of rubrene and its tetrabromo derivative are comparable to those obtained with the water-soluble fluorescer, sulforubrene. This is somewhat surprising since rubrene, a high-melting solid, is not appreciably soluble in cyclohexane. In order to improve the solubility of rubrene, two alkyl substituted rubrene derivatives, bis-hexylrubrene and bis-dodecylrubrene, were prepared, and evaluation of these fluorescers in the solvent-emulsified system gave excellent results. The quantum yield obtained with the bis-hexylrubrene, 8.15%, is the highest efficiency obtained thus far from aqueous chemiluminescence.

The spectral distribution from the emulsified rubrene is very similar to the spectrum of a chemiluminescent reaction in phthalate solvent using rubrene as the fluorescer. In the anthracene derivatives, the spectral distribution from BPEA contrasts with the two alkyl derivatives in that the shorter wavelength peak is missing in the spectra of the derivatives. This may be due to the higher solubility of the derivatives giving rise to more self-absorption. BPEA itself has only slight solubility in cyclohexane.

A number of different surfactant types were screened in the METQ-sulforubrene aqueous reaction (Table 10). The nonionic, polyoxyethylene types appeared to be slightly more effective than the anionic (sulfonate or sulfate) surfactants. The one cationic surfactant tested gave a much lower quantum yield than the other two classes. The length of the polyoxyethylene chain in the nonionic polyether alcohols has little effect on the quantum yield in the METQ-sulforubrene system.

The effect of surfactant concentration on the METQ-sulforubrene system is shown in Table 11. The highest efficiency was found at the lowest concentration used, 0.001M. Very little differences were found up to the highest level used .0089M. To ascertain whether a micelle mechanism is important in this reaction, further studies should be done above and below the critical micelle concentration which is approximately .0001M (18). A study of effect of the sulforubrene fluorescer concentration on the efficiency of the METQ-surfactant system indicated that the highest efficiency was obtained at the highest fluorescer concentration, 0.05M. This is nearly an order of magnitude higher than the optimum concentration normally found in the non-aqueous reactions. Excessive foaming prevented the use of higher levels. It should be noted that the sulforubrene fluorescer used in this study is, in fact, a mixture of at least three components, one or more of which may be the highly efficient in accepting the energy of the chemiluminescent reaction.

A series of experiments using buffer solutions to control the pH of the aqueous reaction were carried out (see Table 13). The highest quantum yield was found at a pH of 3.0 and the lowest at pH 8.4. Light decay rates were slowest at the lowest pH and highest at the highest pH. The efficiency of the best buffered reaction, 3.30%, was significantly lower than the quantum yield of the unbuffered system. This may be caused by a quenching effect of the relatively high buffers used; enough buffer capacity is present to neutralize all the oxalic acid present assuming complete hydrolysis. The use of deuterium oxide as the solvent gave a nearly 50% reduction in efficiency with a small but significant increase in the light decay rate in the isotopic solvent. This suggests that the competitive processes which reduce the quantum yield are enhanced in the deuterium oxide. An enhanced hydrolysis rate in the isotopic solvent could also explain these results.

The role of the surfactant in improving the efficiency of the aqueous METQ-sulforubrene chemiluminescent reaction remains unclear at this writing. However, the effect is substantial and opens the way for the development of much more efficient systems in the future.

Detailed studies of the mode of action of the surfactant will be important in the development of these high light capacity aqueous systems.

2. NON-AQUEOUS REACTIONS

The results summarized in Table 18 indicate that the bis-octyl and bis-dodecyl derivatives of 9,10-bis(phenylethynyl) anthracene (BPEA) gave substantially higher efficiencies in the standard non-aqueous reaction in phthalate ester solvent with the oxalate ester CPPO. The origin of this improved performance was investigated since the structural changes were relatively small to produce such a major impact.

The efficiency of BPEA is limited by its low solubility in dibutyl phthalate. Comparison of the efficiencies of BOBP and BDBP versus BPEA at this concentration limit showed quantum yields of 15.9% and 15.4%, respectively, compared to 12.5% for BPEA. The higher solubility of the alkyl derivatives permitted the optimum concentration to be determined. Increasing the concentration of the oxalate ester at this concentration of BOBP revealed typical concentration quenching with a maximum light capacity of 532 lumen-hours per liter obtained at the highest CPPO level, 0.20 M. BPEA has a maximum light capacity of 300, but this is probably limited by the low solubility of this fluorescer in dibutyl phthalate.

Fluorescent molecules are known from previous work (8) to undergo decomposition during peroxyoxalate chemiluminescent reactions. A reduced rate of fluorescer destruction could then explain the improved performance of the alkyl substituted compounds. Kinetic experiments (Table 19) indicated that the alkyl derivatives, in fact, decompose slightly faster than BPEA itself, thus ruling out this possibility. Reduced fluorescence quenching in the alkyl derivatives was also eliminated as a possible cause since Stern-Vollmer experiments indicated that the fluorescence of both BOBP and BPEA is quenched by the oxalate ester CPPO to the same extent. It has been suggested that differences in the diffusion rates of the larger alkyl-substituted hydrocarbons could explain the higher quantum yields obtained with these compounds (15). In a complex of the key intermediate and the fluorescer a slower diffusion of the fluorescer out of the complex might improve the energy transfer and thereby increase efficiency of this step. Further experimental studies will be needed to clarify the mechanism by which the alkyl BPEA derivatives improve the efficiency of the chemiluminescent reaction.

The use of the N-triflyloxamides in the peroxyoxalate chemiluminescent reaction gave the highest quantum efficiencies ever reported for a non-enzymatic reaction (10). The effect of the structure of a series of these triflyloxamides is summarized in Table 20. The 2,4,5-trichlorophenyl compound was the most efficient (34% quantum yield), but the symmetrical isomer, the 2,4,6-trichlorophenyl derivative, was less than a third as efficient (11%). Steric effects may play a role in lowering the efficiency of the symmetrical isomer. The powerful electron-attracting effect of the triflyl group is particularly evident in the N-alkyl compounds which give quantum

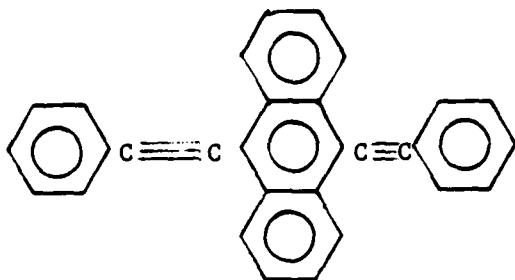
yields in the 1% to 5% range. The corresponding oxalate esters would produce no detectable chemiluminescence. As expected, increasing the length of the alkyl chain between the oxamide nitrogen and an electron-attracting group such as ester or halogen significantly reduces the efficiency of the reaction.

Heteroaromatic triflyloxamides such as the 2-chloro-3-pyridyl (34) gave good chemiluminescence in dibutyl phthalate, but the presence of the basic nitrogen often tended to reduce lifetime and efficiencies in several heteroaromatic oxalate esters (Table 21).

IV. SYNTHESIS OF NEW CHEMILUMINESCENT MATERIALS

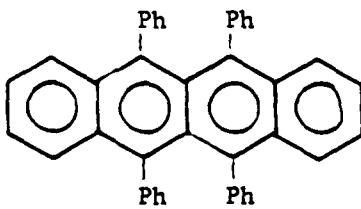
A. FLUORESCERS: DESIGN AND SYNTHESIS

Efficient oxalate ester chemiluminescence requires a fluorescer which has a high fluorescence quantum yield. In addition, the fluorescer should emit radiation in the green to orange spectral region where the human eye is most sensitive. The fluorescer must also be capable of efficient complex formation with the key chemiluminescent intermediate to permit efficient trapping of the energy released from the decomposition of the intermediate. Polycyclic aromatic hydrocarbons such as 9,10-bis(phenylethynyl)-anthracene (BPEA) and its derivatives have been previously employed successfully in non-aqueous chemical light systems (2-6).



9,10-Bis(phenylethynyl)anthracene (BPEA)

Another polycyclic aromatic hydrocarbon, rubrene, has also been found to be highly efficient in a non-aqueous chemical light system (4). Rubrene was found to give a higher chemiluminescent efficiency than BPEA in dilute solution, due to its higher excitation yield. Rubrene, however, at high concentrations of oxalate ester exhibits shorter lifetimes due to its greater ease of photooxidation compared to BPEA in non-aqueous systems. Nevertheless, as has been seen in aqueous surfactant systems, rubrene and several of its derivatives exhibit lifetimes greater than BPEA derivatives. A reduced rate of photooxidation of rubrene in the aqueous surfactant system may be one of the factors responsible for the increased efficiency.

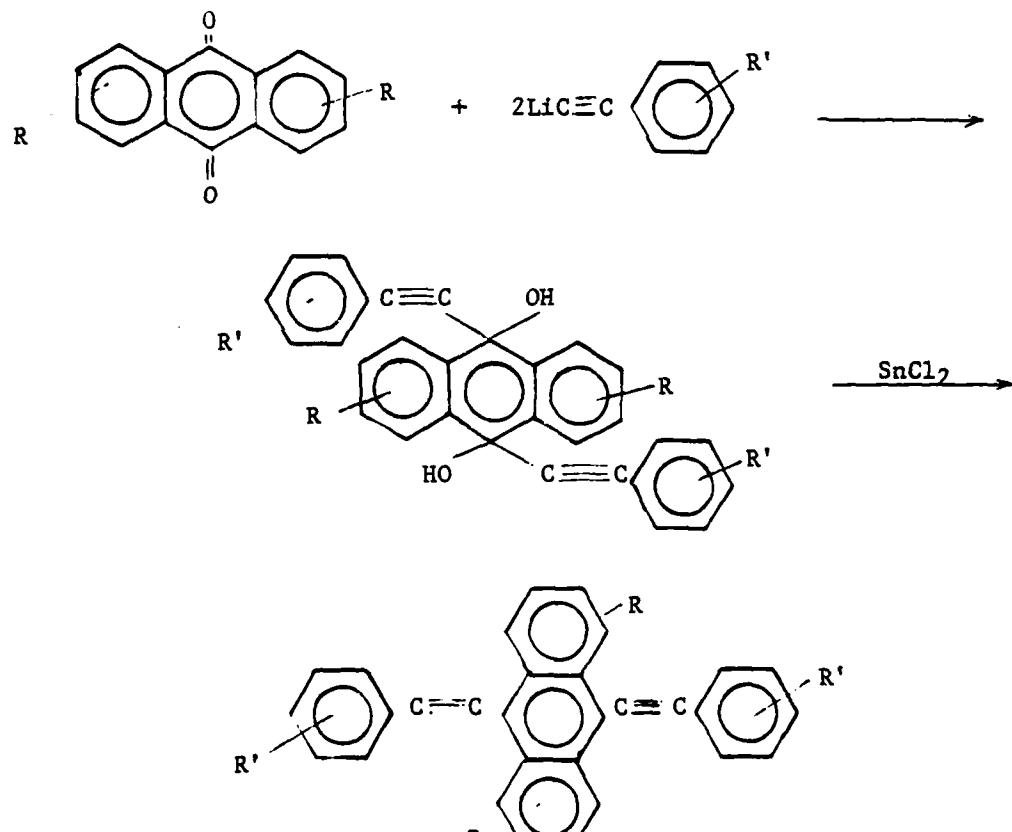


Rubrene

Thus, one approach to a water-soluble fluorescer is to modify the structure of known efficient fluorescers such as BPEA or rubrene to introduce water solubility via the addition of substituents such as sulfonic acid salts, polyoxyethylene chains and quaternary ammonium salts to the acene ring or to the pendant phenyl rings.

The preparation of BPEA is shown in Scheme 1. Treatment of anthraquinone ($R=H$) with two moles of lithium phenylacetylide ($R'=H$) in dioxane yields the diol, which can be isolated and reduced with stannous chloride dihydrate (16) or reduced *in situ* and the product precipitated by the addition of glacial acetic acid and dilute sulfuric acid (17). The majority of BPEA derivatives in this report were prepared by the latter method.

Scheme 1



BPEA: $R = R' = H$

The direct introduction of water-solubilizing functional groups, for example, a sulfonic acid group via sulfonation, onto BPEA was ruled out due to the presence of the particularly labile acetylenic linkage in strongly acidic media. Furthermore, the use of anthraquinone or phenylacetylene precursors already possessing ionic functionality (e.g., R or R'=SO₃Na) presented solubility problems (11). Therefore, the course of modification chosen was to prepare and utilize anthraquinone and/or phenylacetylene precursors having "pro" water-soluble groups which would be inert to the conditions of the BPEA synthesis reaction (Scheme 1). These groups would be converted to water-solubilizing groups in the last step, by hydrolysis or quaternization, to yield a water-soluble BPEA derivative.

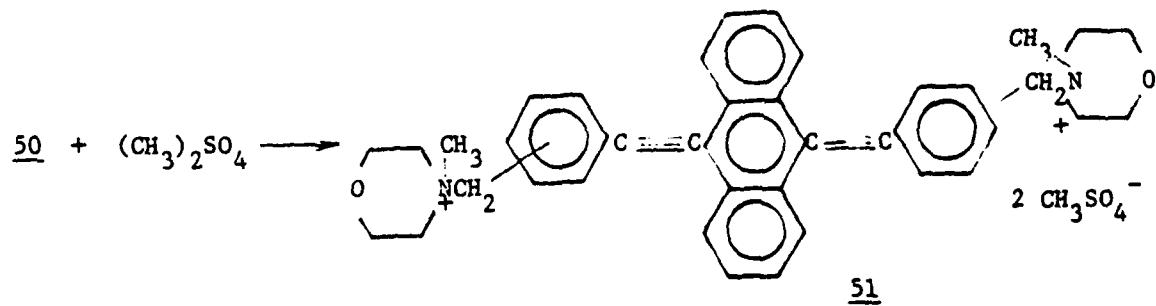
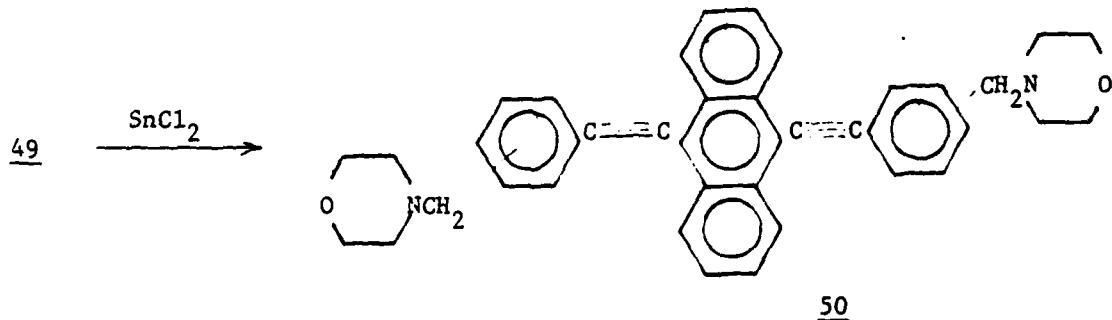
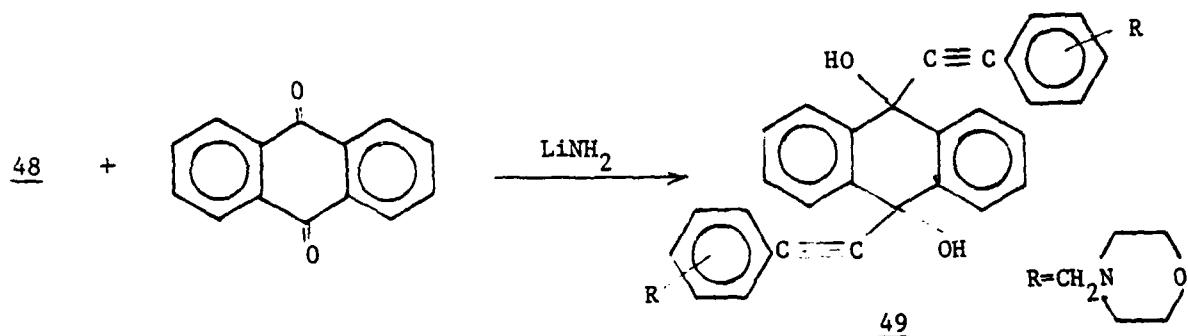
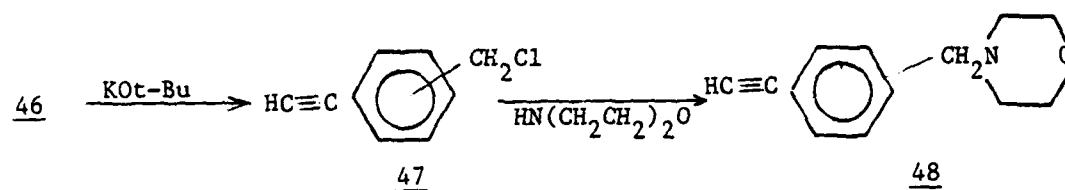
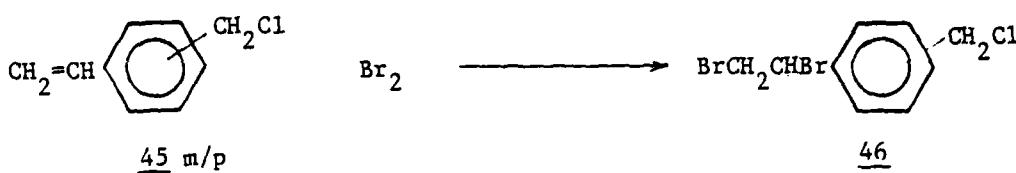
Additionally, it was desirable to prepare a BPEA derivative containing hydroxyl groups (R or R'=OH) which could be alkylated with polyoxyethylene chains or other alkylating agents to introduce water-solubility. This approach provided the benefit of working with non-ionic organic molecules throughout most of the reaction sequence, which could be more easily purified by crystallization and characterized than ionic derivatives.

The majority of the fluorescers were prepared by using the phenylacetylene derivative as that precursor which incorporated the "pro" water-soluble functional group. Consequently, this led to the introduction of two water-soluble functionalities in the final product, which was found preferable from solubility considerations. Conversely, anthraquinone precursors containing two such groups were found to be not so readily available and often insufficiently soluble in the reaction medium, although some were prepared.

The aforementioned approaches are now illustrated in the examples which follow.

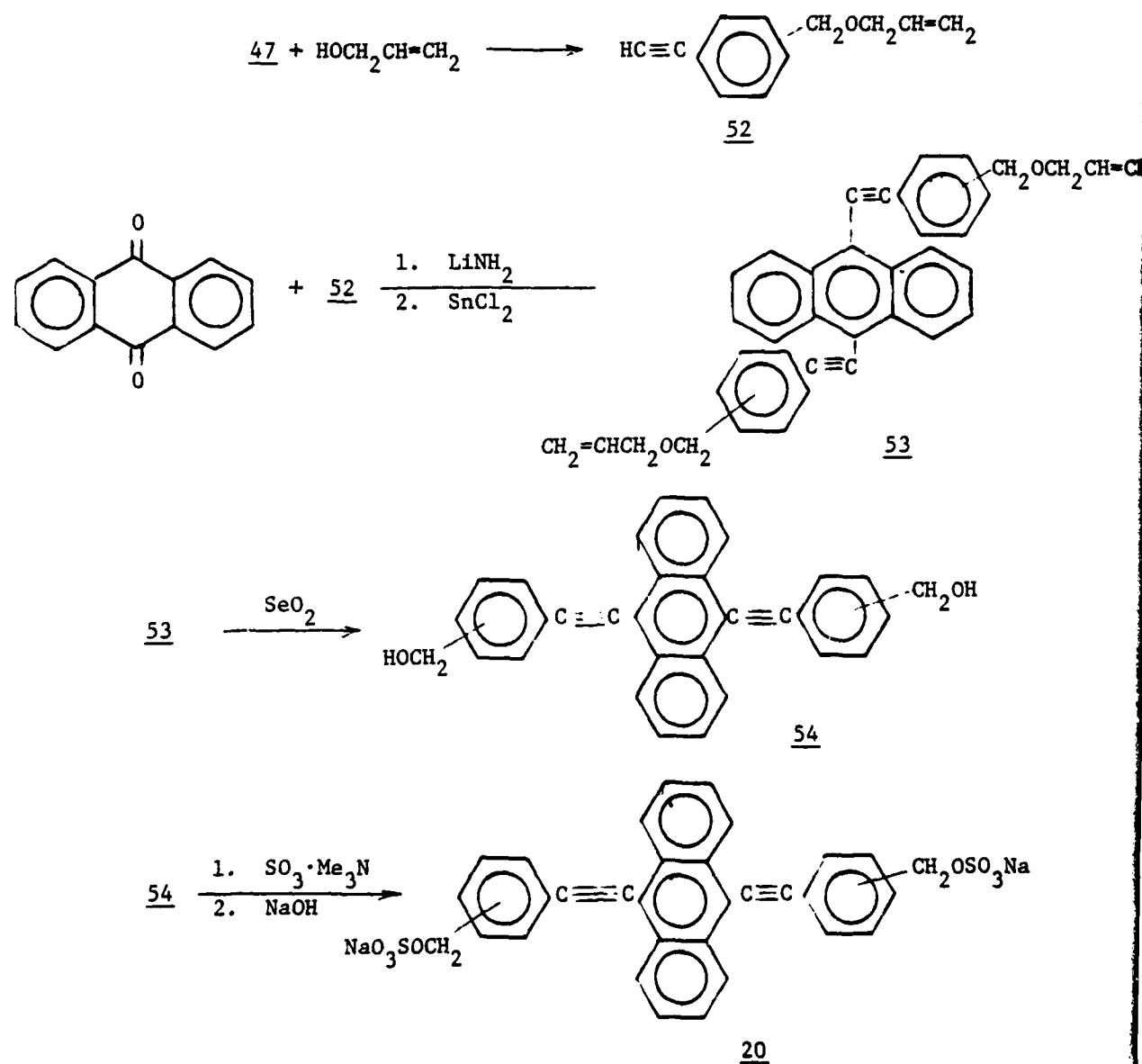
In Scheme 2, chloromethylstyrene, 45, was brominated to the dibromo derivative, 46, which was then dehydrobrominated to give chloromethylphenylacetylene, 47. Compound 47 was condensed with morpholine to give the desired morpholinomethylphenylacetylene precursor, 48. By employing 48 in the reaction sequence illustrated in Scheme 1, the bis-morpholinomethyl BPEA derivative, 50, was obtained. Quaternization with dimethyl sulfate afforded 51, which was soluble in water, giving a strong green fluorescence. It should be noted that the chloromethylstyrene, 45, was actually a mixture of the meta and para isomers as received from the supplier. All compounds derived from this material reflect this isomer distribution.

Scheme 2



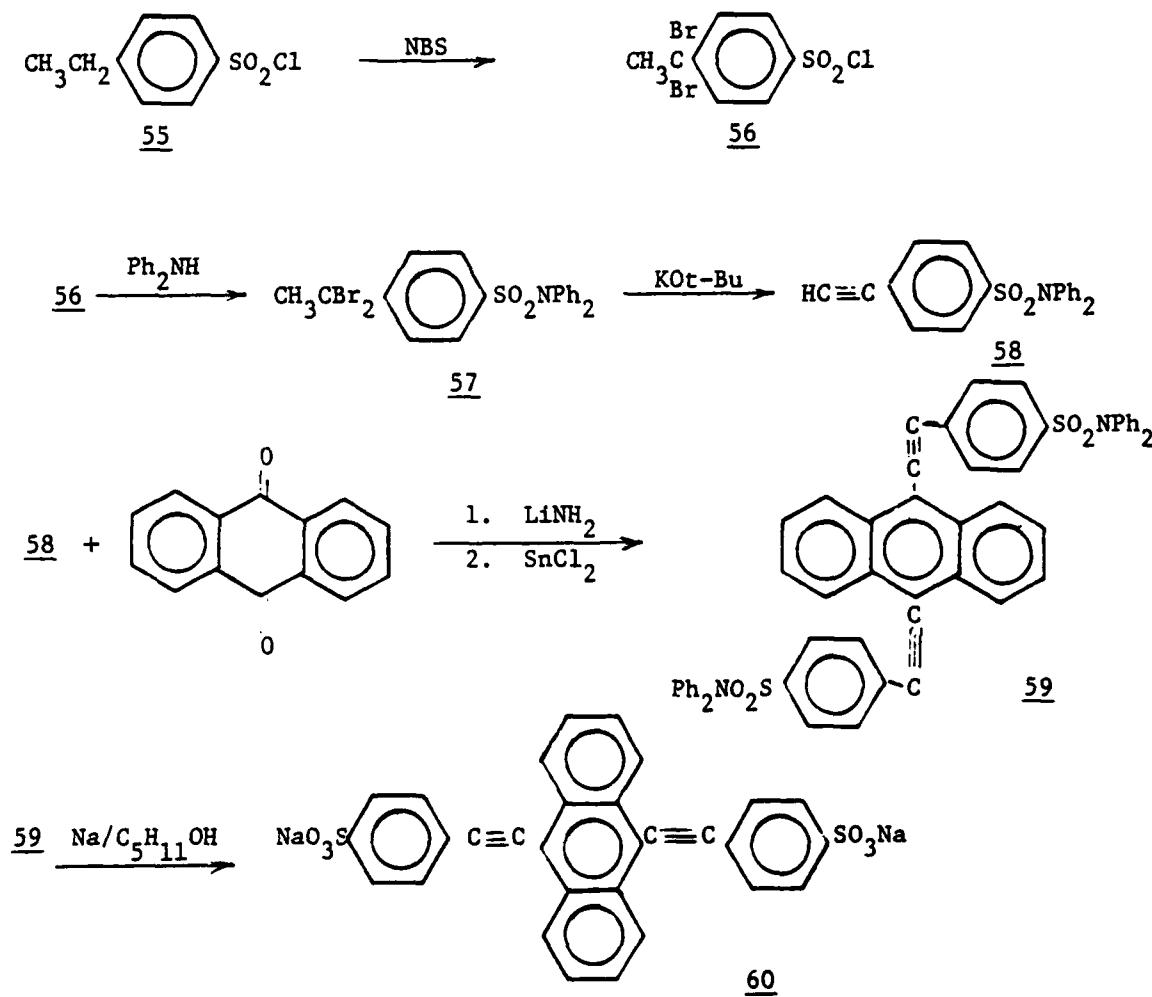
Scheme 3 illustrates the synthesis of the bis-sulfate salt BPEA derivative, 20. Chloromethylphenylacetylene, 47, was converted to allyloxyphenylacetylene, 52, with allyl alcohol (18). The allyloxyphenyl BPEA derivative, 53, was then prepared via the conventional route. Cleavage of allyl groups with selenium dioxide (19) gave bis-hydroxymethyl-BPEA, 54. Selenium dioxide was used because two more common methods, the rearrangement with $KOt\text{-}Bu/DMSO$ (20) or a rhodium catalyst (21) to the acid-labile propenyl group, did not succeed. Condensation of 54 with the sulfur trioxide-trimethylamine complex, followed by the addition of NaOH gave the desired water-soluble green fluorescer, 20. In this particular example, it was necessary to protect the hydroxyl group since addition of lithium amide to hydroxymethylphenylacetylene to form the acetylidyde would have caused the precipitation of the lithium salt, thereby inhibiting the reaction.

Scheme 3



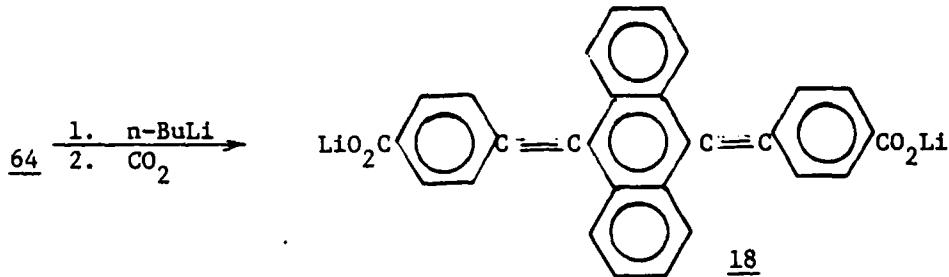
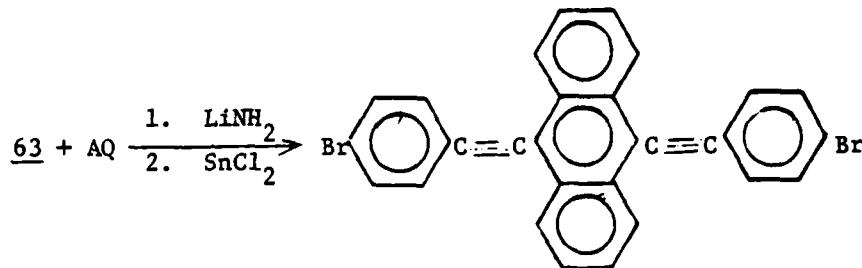
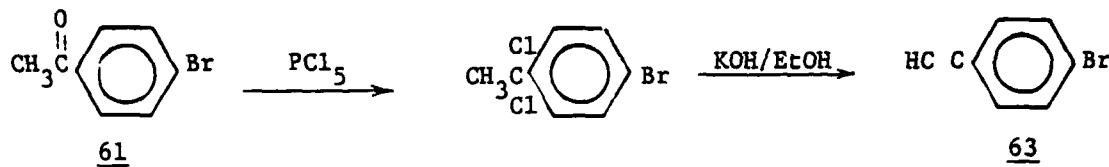
The attempted preparation of an analogous derivative of BPEA, 60, is illustrated in Scheme 4. Ethylbenzenesulfonyl chloride, 55, was brominated to the gem dibromide, 56, which was then treated with diphenylamine to give sulfonamide 57. The sulfonamide was then dehydrobrominated to give 4-ethynyl-N,N-diphenylbenzenesulfonamide, 58. The BPEA derivative, 59, was then prepared by the conventional route. The use of an N,N-diphenylsulfonamide as the "pro" water-soluble group was chosen for two reasons. First, although a sulfonate ester could be very easily hydrolyzed with base to yield the desired bis-sulfo salt (22), it would also be susceptible to attack by lithium amide, possibly leading to very low yields (see below). Secondly, base hydrolysis of N,N-diaryl sulfonamides has been found to proceed, whereas N,N-dialkyl sulfonamides have been found to be inert (23). Hydrolysis of 59 using Na/i-amyl alcohol led to a water-soluble, green fluorescent solid, probably 60, which could not be obtained pure.

Scheme 4



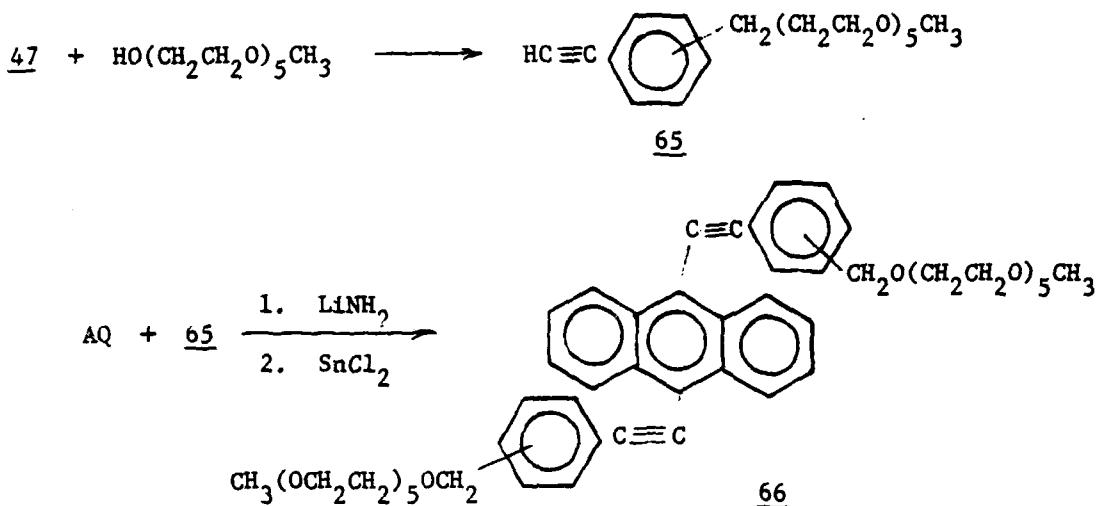
The preparation of a bis-carboxylate BPEA derivative, 18, was attempted via Scheme 5. p-Bromoacetophenone, 61, was chlorinated with phosphorus pentachloride to the gem-dichloro derivative, 62, which was then dehydrochlorinated using KOH/ethanol to obtain p-bromophenylacetylene, 63. The acetylide was condensed with anthraquinone (AQ) and reduced to give dibromo-BPEA (BRBPEA), 64. Metal-halogen exchange with n-butyllithium, followed by carboxylation with carbon dioxide gas generated a water-soluble green fluorescent solid, presumably 18, which was only weakly chemiluminescent in water.

Scheme 5



The synthesis of a non-ionic water-soluble BPEA derivative is shown in Scheme 6. Chloromethylphenylacetylene, 47, and pentaoxahexadecanol were condensed (18), giving the pentaethyleneoxy acetylenic derivative, 65. By the conventional scheme, bis-pentaethyleneoxy-BPEA, 66, was obtained as an oil, even after HPLC purification. This lack of crystallinity is a common physical property attributed to polyoxyethylene chains. The compound was highly chemiluminescent in organic solvents and moderately chemiluminescent in the aqueous system.

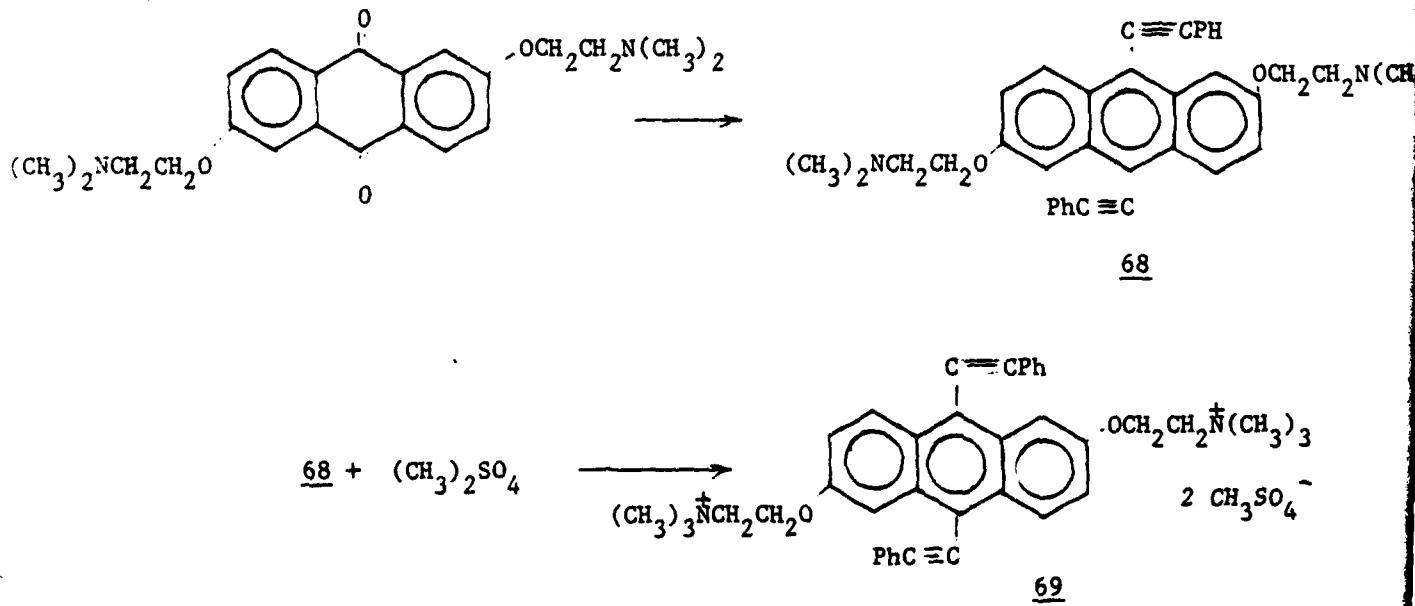
Scheme 6



The next several syntheses comprise those BPEA derivatives prepared from a substituted anthraquinone precursor.

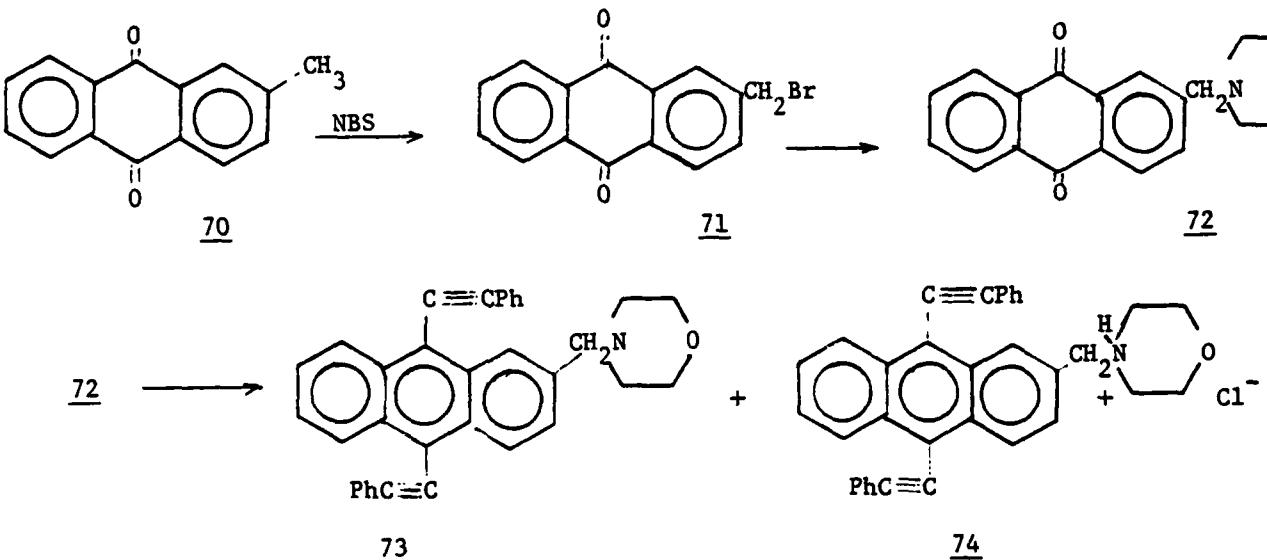
One of the cationic quaternary BPEA derivatives prepared is shown in Scheme 7. The anthraquinone, 67 (Aldrich, from the hydrochloride-dihydrate), was condensed with lithium phenylacetylide and reduced to give 2,6-bis[N,N-dimethylaminoethoxy]-9,10-bis(phenylethyanyl)anthracene, 68. Quaternization using dimethyl sulfate afforded the bis quaternary ammonium salt, 69, which was found to be moderately chemiluminescent in water in the presence of a surfactant.

Scheme 7



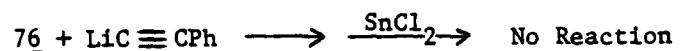
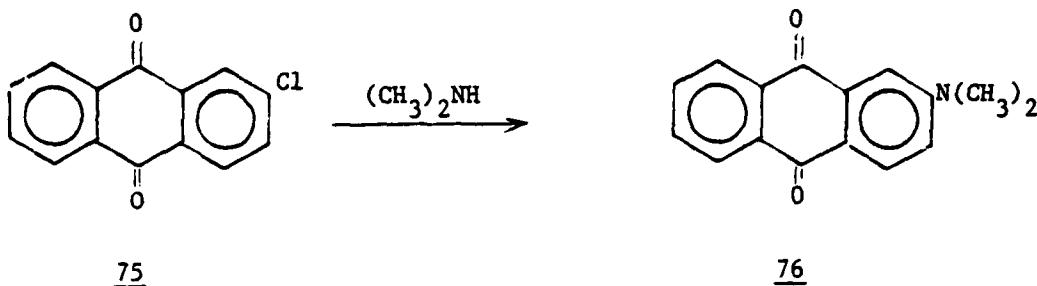
Scheme 8 illustrates the attempted synthesis of another amino-BPEA derivative capable of being quaternized to achieve water-solubility. 2-Methylanthraquinone, 70, was brominated with N-bromosuccinimide (NBS) to the bromomethyl derivative, 71, which was then condensed with morpholine, giving the 2-morpholinomethyl derivative, 72. Conversion to the BPEA derivative via the conventional route gave a mixture of the morpholinomethyl-BPEA product, 49, and its hydrochloride salt, 74. Purification of this mixture was unsuccessful; nevertheless it was weakly chemiluminescent in water.

Scheme 8



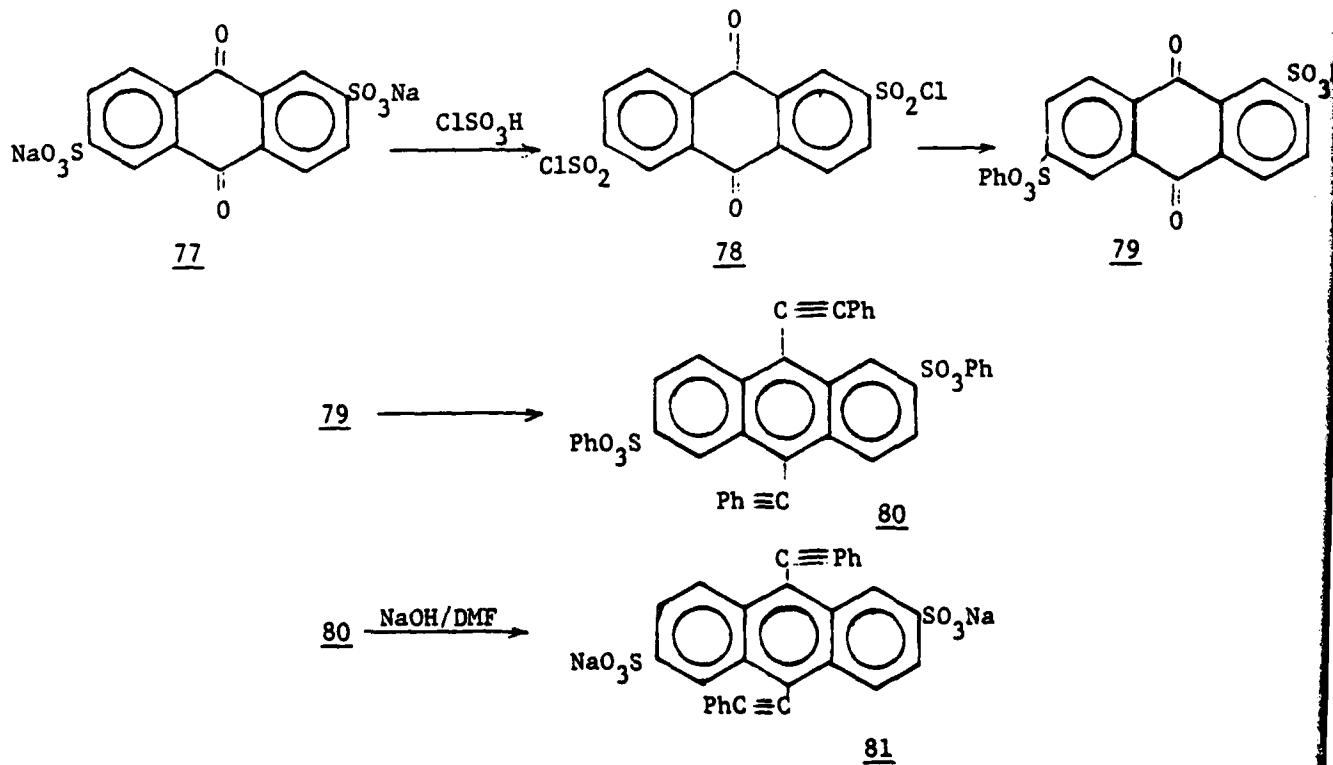
Scheme 9 illustrates the attempted synthesis of 2-dimethylamino-BPEA. 2-Chloroanthraquinone, 75, was heated at 200 C. under pressure in the presence of potassium acetate, copper powder, cupric acetate and dimethylamine (33), affording 2-dimethylaminoanthraquinone, 76. The phenylethynylation of 76, however, was not successful. The electron donating ability of the dimethylamino group attached to the anthracene nucleus may have been responsible for reducing the susceptibility of the carbonyl groups towards phenylethynylation. It is interesting to note that this was not a problem in the two previous examples where the effect of the amino functionality was insulated by an ethyleneoxy and a methylene bridge, and the reactions proceeded.

Scheme 9



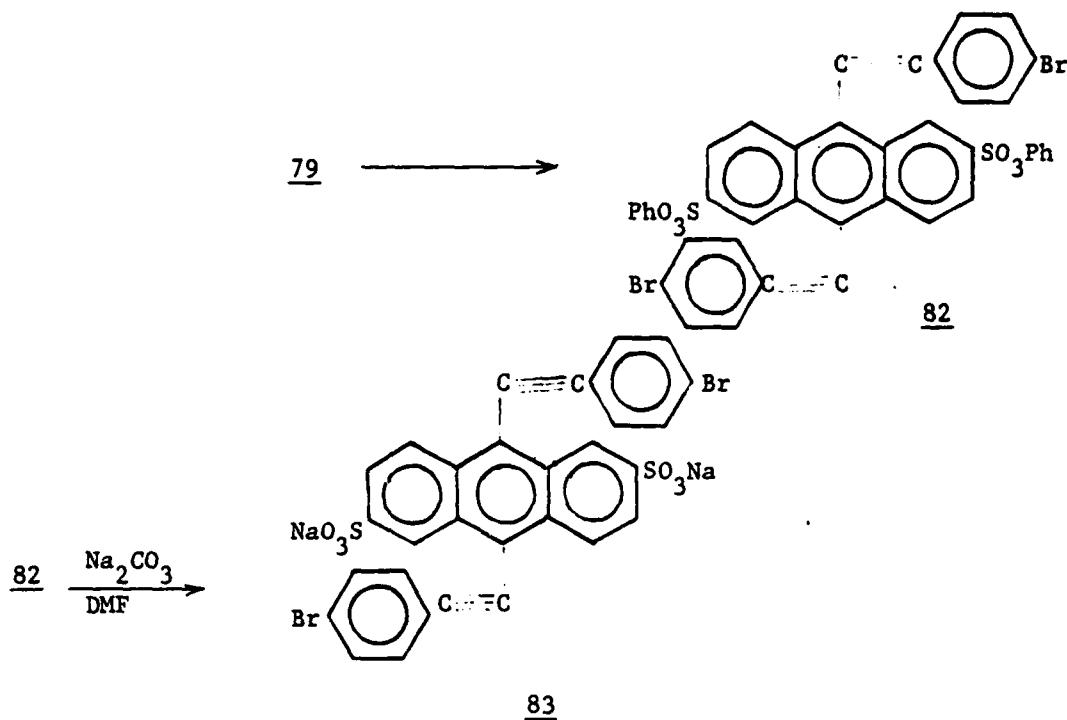
The attempted synthesis of a bis-sulfonic acid derivative of BPEA, with the sulfate groups on the anthracene nucleus, is shown in Scheme 10. Anthraquinone-2,6-disulfonic acid, disodium salt, 77, was converted to the sulfonyl chloride, 78 (25), which was then esterified with phenol to the bis sulfonate ester, 79. Conversion of 79 to the BPEA derivative gave a very low yield of 80, possibly due to the susceptibility of the sulfonate ester to attack by lithium phenylacetylide or lithium amide. The attempted hydrolysis of 56 using NaOH/DMF at reflux gave a semi-solid product, which was not totally pure even after HPLC. However, the crude material was entirely water-soluble, giving a green fluorescent solution.

Scheme 10



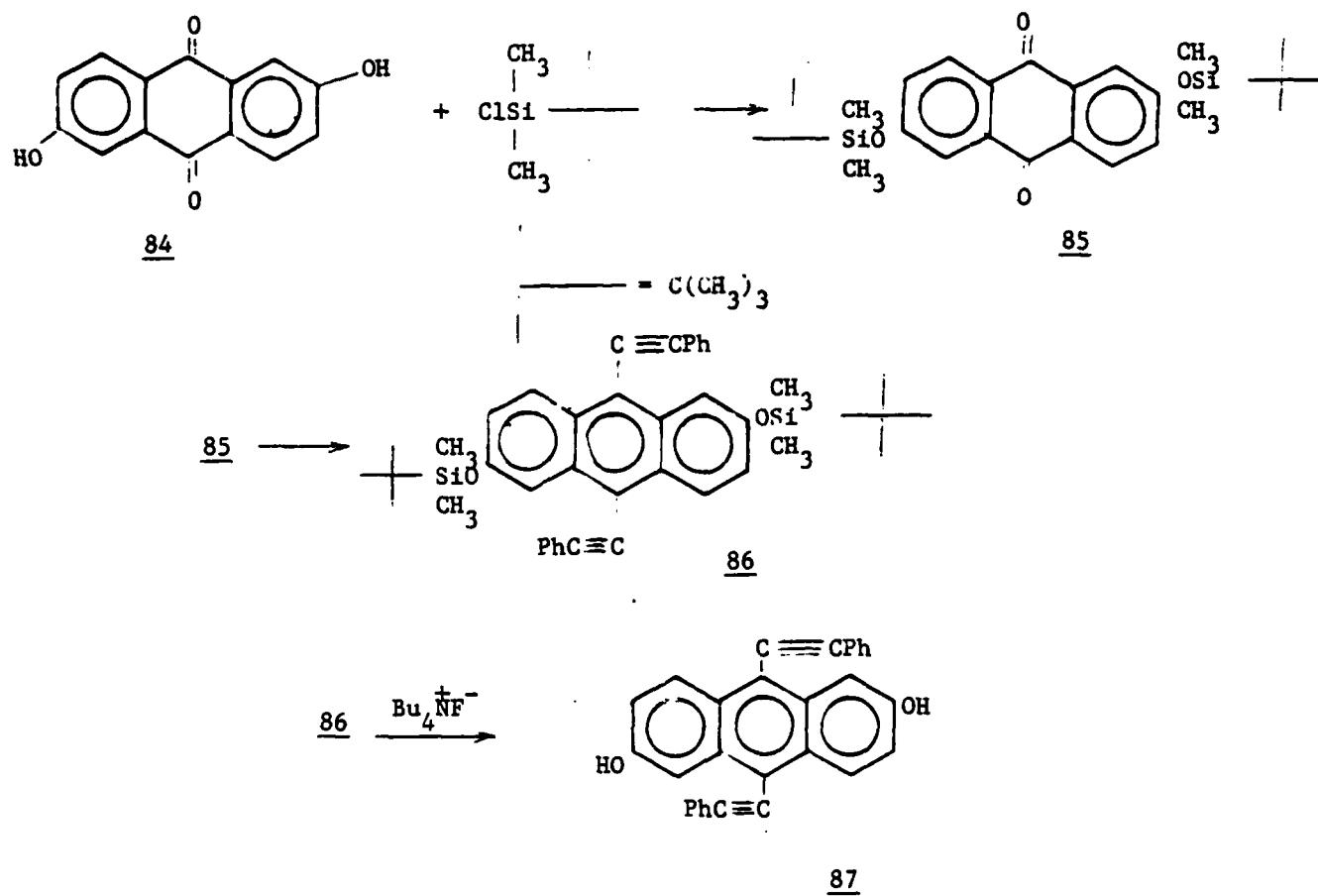
The dibromo analog of 80, 82, was also prepared by the route shown in Scheme 10. Hydrolysis of 82 using sodium carbonate in DMF at reflux gave a product which showed two major fluorescent components indicative of water-soluble salts by reverse-phase TLC. An aliquot of the product solution was dissolved in water, yielding a green fluorescent solution (Scheme 11).

Scheme 11



As previously mentioned, it was desirable to prepare a BPEA derivative containing free hydroxyl groups as an intermediate which could be more easily converted to any number of water-soluble fluorescers. The synthesis of 2,6-dihydroxy-BPEA is illustrated in Scheme 12. The hydroxyl groups of 2,6-dihydroxyanthraquinone, 84, were first protected using t-butyldimethylchlorosilane (26); free hydroxyl would interfere in the phenylethynylation step. Chlorotrimethylsilane (TMS) had been initially tried but was unsuccessful in that very little product, if any, was obtained. The MEM protecting group (27) was also tried. Although its use enabled phenylethynylation to proceed smoothly to give a good yield of the bis MEM ether of BPEA (analog of 85), cleavage of this ether using the literature methods (36) was unsuccessful. Hydrolysis was initiated using methanesulfonic acid in aqueous alcohol but could not be "pushed" to completion. The bis-silyl ether, 85, was then smoothly converted by the usual route to the bis-silyl BPEA ether, 86. Removal of the protecting groups using tetra-n-butylammonium fluoride in THF yielded the desired product, DHBPEA, 87.

Scheme 12



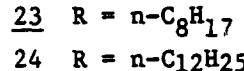
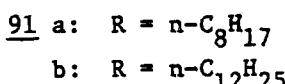
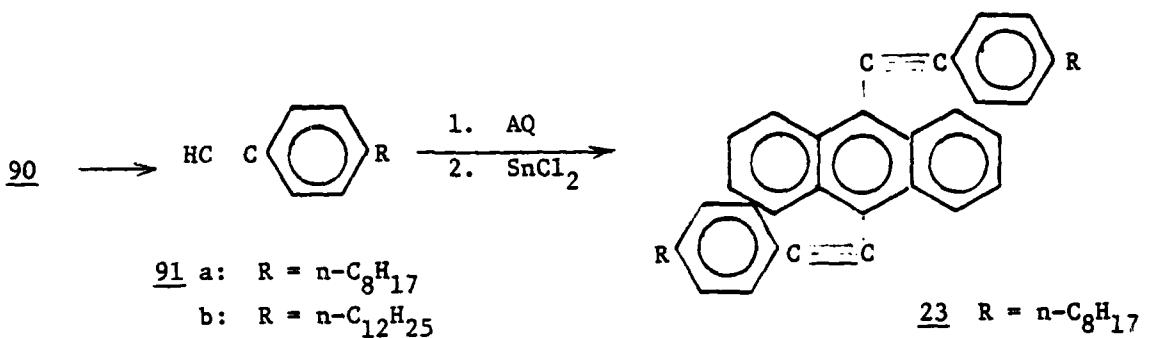
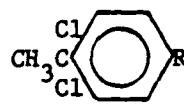
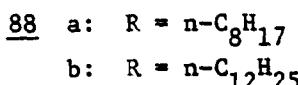
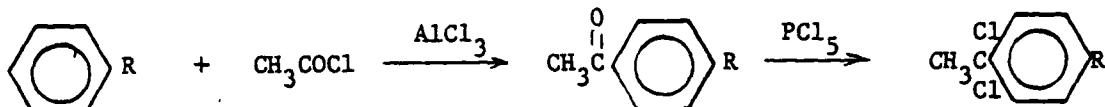
Potential uses of 87 include alkylation with the sulfur trioxide-triethylamine complex or sodium 2-bromoethanesulfonate and conversion to a bis-polyoxyethylene BPEA similar to 66.

Based upon the encouraging aqueous chemiluminescent quantum yields and light capacities obtained when surfactants were added to the chemiluminescent systems, consideration was given to the preparation of fluorescers which could be more readily emulsified in the aqueous reaction mixture than BPEA, e.g., fluorescers containing a long alkyl chain. Such derivatives were expected to have lower melting points, be more soluble in hydrocarbon solvents, and be emulsified readily.

Two such BPEA derivatives were prepared as illustrated in Scheme 13. The appropriate alkylbenzene, either 88a or 88b, was acylated under Friedel-Crafts conditions giving the alkylated acetophenone derivatives, 89, which were chlorinated with phosphorus pentachloride and dehydrochlorinated using $\text{KOT-Bu}/\text{THF}$ to yield the desired alkylated phenylacetylenes, 91. Treatment of anthraquinone with the

respective lithium phenylacetylide gave on reduction either the bis-n-octyl-BPEA, 23 (BOBPEA), or the bis-n-dodecyl-BPEA, 24 (BDDBPEA).

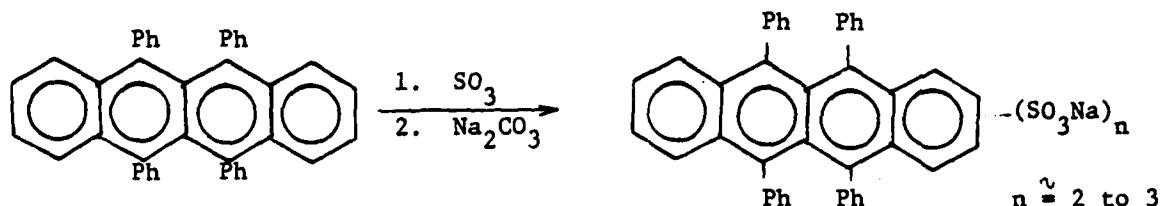
Scheme 13



However, BOBPEA was only veryweakly chemiluminescent in water, even in the presence of a surfactant. These fluorescers, however, produced an interesting sidelight. When tested in the phthalate ester system, they both exhibited light capacities ca. 16%-30% higher than BPEA and gave higher quantum yields. The reasons for this improved efficiency are being investigated.

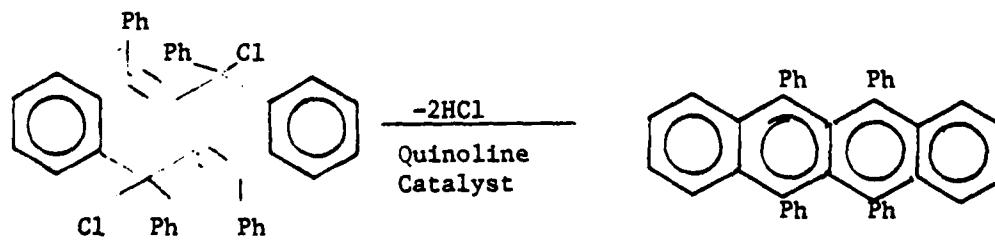
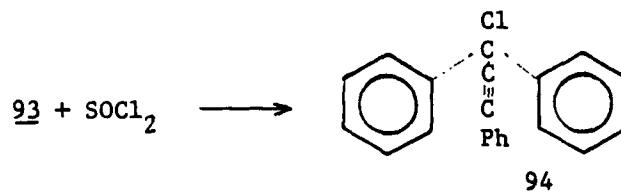
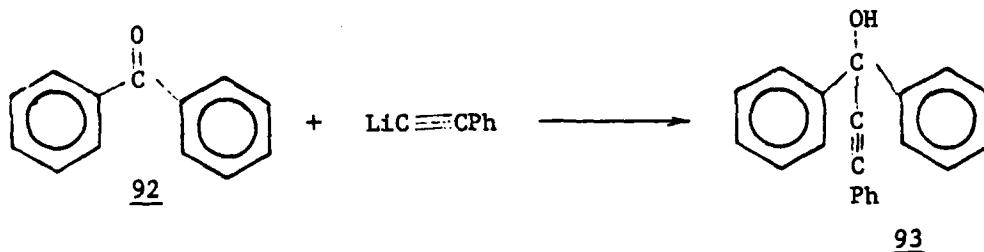
In addition to BPEA derivatives, water-soluble and/or water-dispersible rubrene derivatives have been prepared. Since rubrene is commercially available, the most direct route to water solubilization was by direct sulfonation. However, the literature (28) indicated that the use of usual sulfonation conditions (sulfuric acid) led to the formation of side products, such as a cyclic pseudorubrene and an endoperoxide derivative of rubrene. Direct sulfonation of rubrene (Scheme 14) gave a highly chemiluminescent, water-soluble rubrene derivative having the tentatively assigned structure, 3. The sulfonation was carried out in an ice bath using sulfur trioxide and methylene chloride as the solvent. The literature (37) indicated that the sulfur trioxide should be distilled before use. TLC of the isolated fluorescent product showed a complex mixture. Microanalysis indicated an average of two to three sulfonate groups per rubrene molecule. Repeated recrystallizations and/or preparative HPLC were unsuccessful in providing a single fluorescent species. Also, the crude product mixture always exhibited the highest quantum yield whereas resultant, somewhat purer, product mixtures were consistently lower, possibly suggesting a synergistic effect in the crude mixture.

Scheme 14

3 Sulforubrene

As a result of these difficulties, an alternate route to the preparation of water-soluble rubrene derivatives was pursued. Scheme 15 illustrates the preparation of rubrene according to the original method of Wittig (29). Treatment of benzophenone, 92, with lithium phenylacetylide affords the carbinol, 93. The carbinol is then converted to the propargyl chloride derivative, 94, which is then dimerized with loss of HCl in the presence of quinoline to give rubrene (29,30). The Wittig procedure used no solvent in the dimerization step, and a 20% yield of rubrene was realized. Modification of this procedure by using chlorobenzene as a solvent during this step increased the yields to 40%-50%.

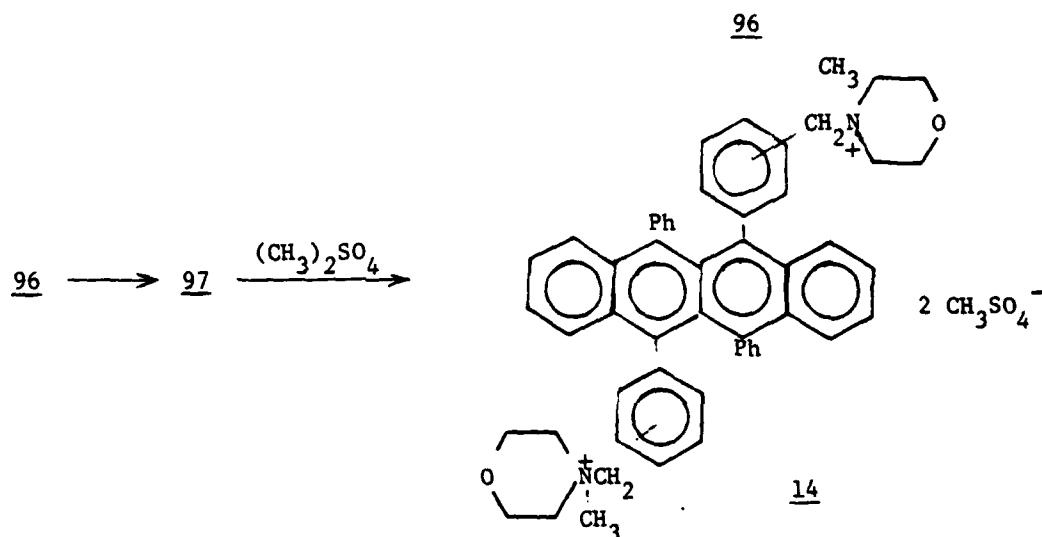
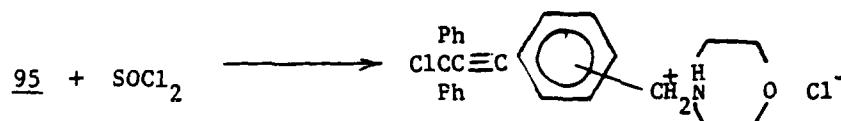
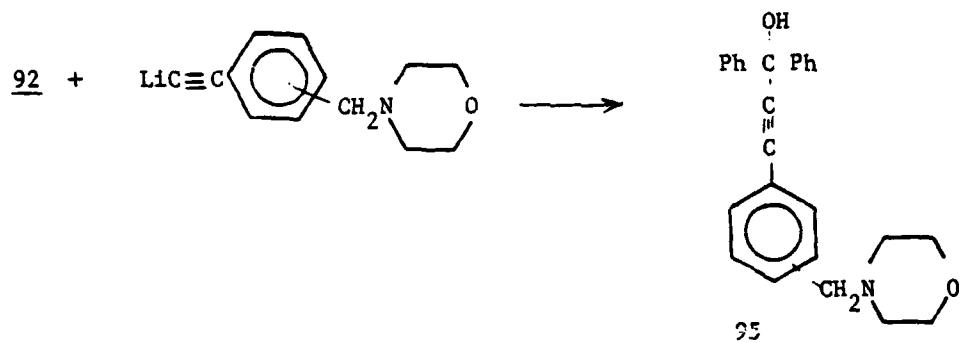
Scheme 15



This synthetic route affords the options of employing either a substituted benzophenone (giving a di-substituted rubrene), a substituted phenylacetylene (also disubstitution) or both, giving a tetrasubstituted rubrene. When 3,3'-disubstituted benzophenones were used, the dimerization could give rise to three isomers, whereas the use of a 4,4'- precursor gave only one. This, coupled with the fact that intermediates were generally not purified, often gave rise to mixtures of products, from which the major product would be isolated by HPLC, giving yields no greater than 50%. The solubility, availability, and ease of preparation of either the benzophenone or phenylacetylene intermediates were the same, so both methods were used. The following examples illustrate those rubrene derivatives which were prepared.

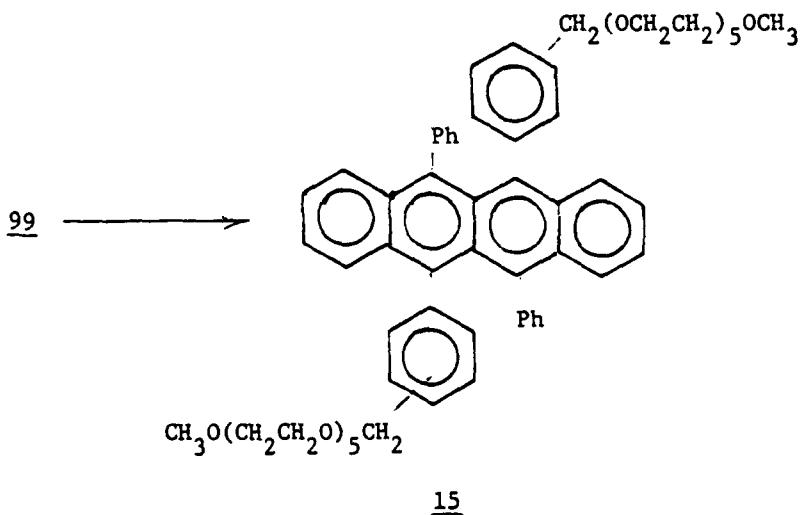
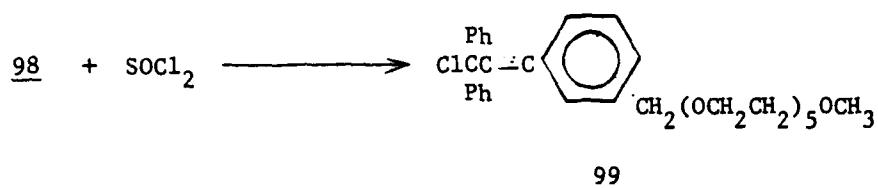
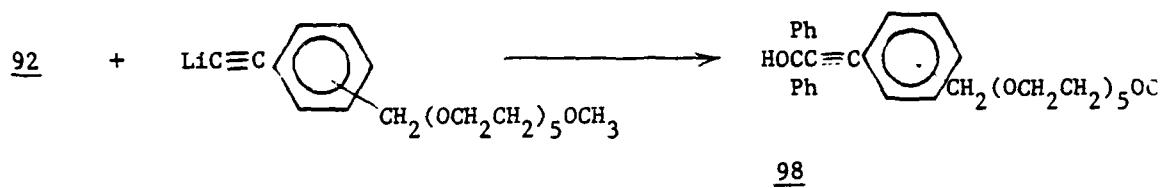
The synthesis of the bis-morpholinomethylrubrene derivative, 97, is shown in Scheme 16. Benzophenone (92) was condensed with morpholinomethyl phenylacetylidyne, giving the carbinol, 95, which was converted to the chloride, 96 (as the hydrochloride salt). This compound was dimerized by refluxing a solution of 96 in DMF in the presence of silica gel to give the bis-morpholinomethylrubrene derivative, 97, as the tertiary amine. Quaternization afforded the water-soluble rubrene, 14.

Scheme 16



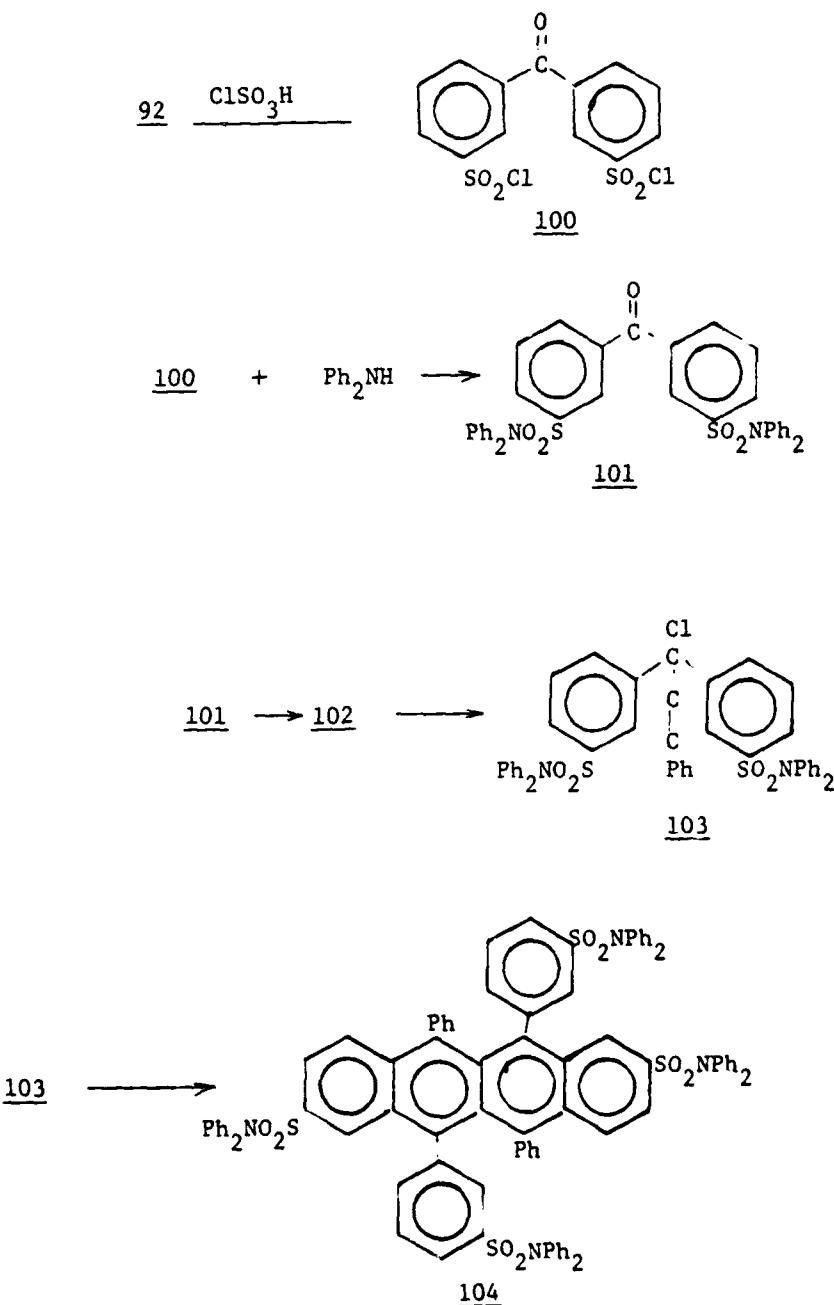
Scheme 17 illustrates the synthesis of the bis-pentaethyleneoxy rubrene derivative, 15. Benzophenone (92) and pentaethyleneoxyphenylacetylide were condensed, giving the carbinol, 98, which was converted to the chloride, 99. Dimerization of the chloride gave a mixture of orange-red fluorescers. Purification by preparative HPLC gave a fraction of high purity which exhibited good chemiluminescence in the aqueous/surfactant system and was identified as the desired product, 15.

Scheme 17

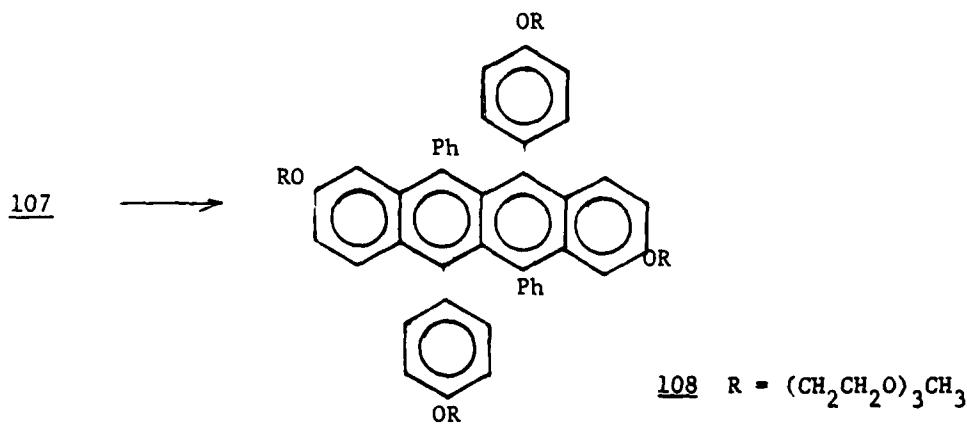
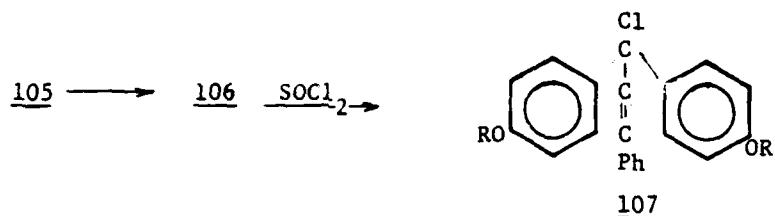
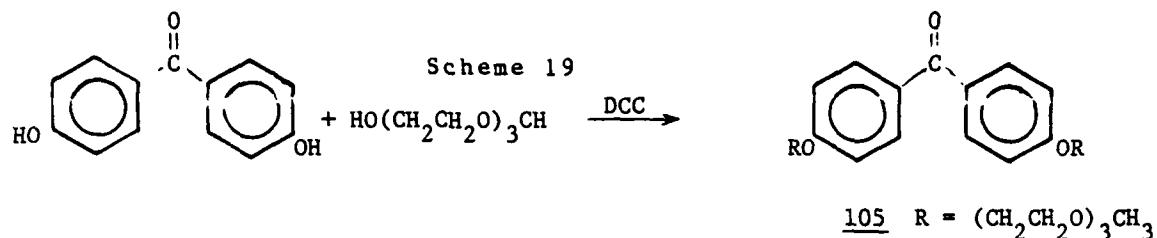


Scheme 18 illustrates the synthesis of a tetra-substituted rubrene derivative. The tetra-sulfonamide was prepared with the objective of hydrolytically cleaving the sulfonamide groups (23) in the last step to sodium sulfonate groups, thereby rendering it water soluble. Benzophenone was chlorosulfonated at the meta positions with chlorosulfonic acid (31) giving the bis-sulfonyl chloride, 100, which was converted with diphenylamine to the bis-sulfonamide, 101. The bis-sulfonamide was condensed with lithium phenylacetylide to give the carbinol, 102, which was converted to the chloride, 103, and then dimerized to the tetra-sulfonamide rubrene, 104. Cleavage of the sulfonamide groups to give a tetra-sodium sulfonate salt would be required to introduce water solubility.

Scheme 18

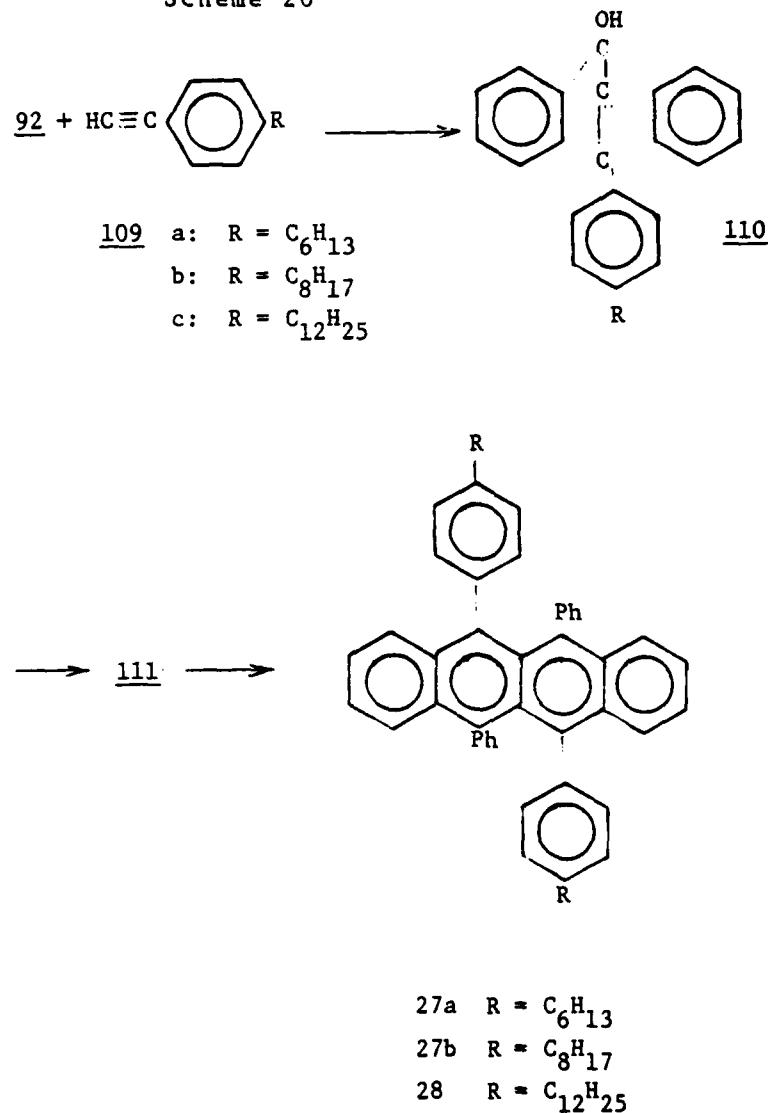


Scheme 19 shows the synthesis of a non-ionic tetra-substituted water-soluble rubrene derivative, 108. 4,4'-Dihydroxybenzophenone was etherified with methoxytriglycol using dicyclohexylcarbodiimide (DCC) to the bis-polyether benzophenone, 105. This was then converted by the same synthetic route as in the previous example to the tetra-substituted rubrene derivative, 108. It was isolated as an oil and found to be highly chemiluminescent in water and to possess a long lifetime.



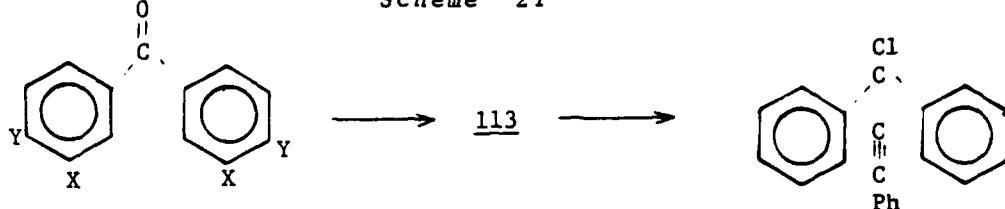
As in the case of the long chain n-alkyl-BPEA derivatives (see above), several analogous rubrene derivatives were prepared with the objective of achieving water dispersibility as a result of the n-alkyl chains, as can be seen in Scheme 20. Benzophenone treated with the appropriate alkylphenylacetylide (109) gave the carbinols, 110, which were converted to the chlorides and dimerized to the alkylated rubrene derivatives, 27a, 27b and 28. All three fluorescers exhibited intense red chemiluminescence in the cyclohexane/water/surfactant emulsion.

Scheme 20

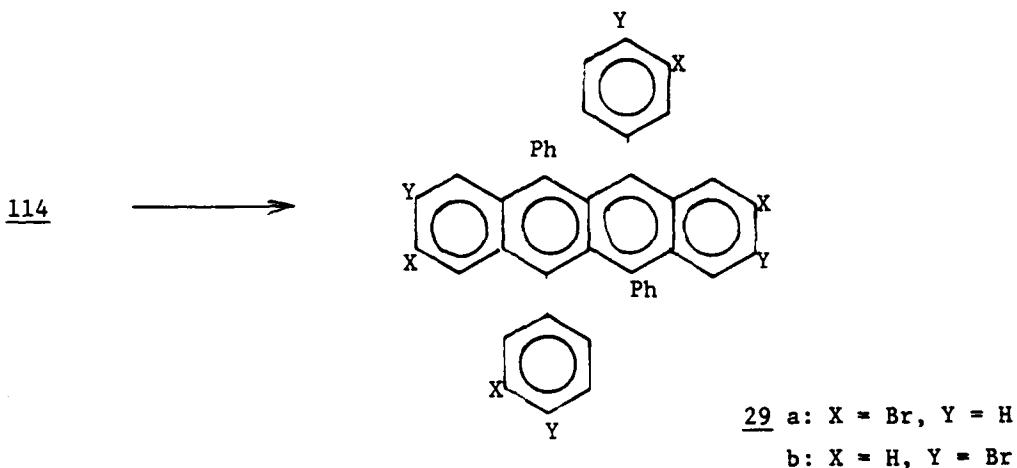


Two tetrabromorubrene isomers, 29a and 29b, were prepared as illustrated in Scheme 21.

Scheme 21



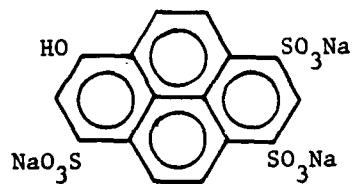
112 a: X = Br, Y = H
b: X = I, Y = Br

114

29 a: X = Br, Y = H
b: X = H, Y = Br

Either 3,3'-dibromobenzophenone, 112a, or 4,4'-dibromobenzophenone, 112b, was phenylethynylated to the carbinol, 113, which was converted to the chloride, 114, and dimerized to give the corresponding tetrabromorubrene isomer. Although each isomer showed only one spot by TLC, mass spectral analyses revealed the presence of chlorotribromo- and dichlorodibromo- impurities in small amounts. Qualitatively, 27b showed strong orange-red chemiluminescence in cyclohexane/water/surfactant emulsions.

At an early stage in the water-soluble program (11), the water-soluble fluorescer HPTS was used for the quantitative testing of water-soluble oxalate esters.

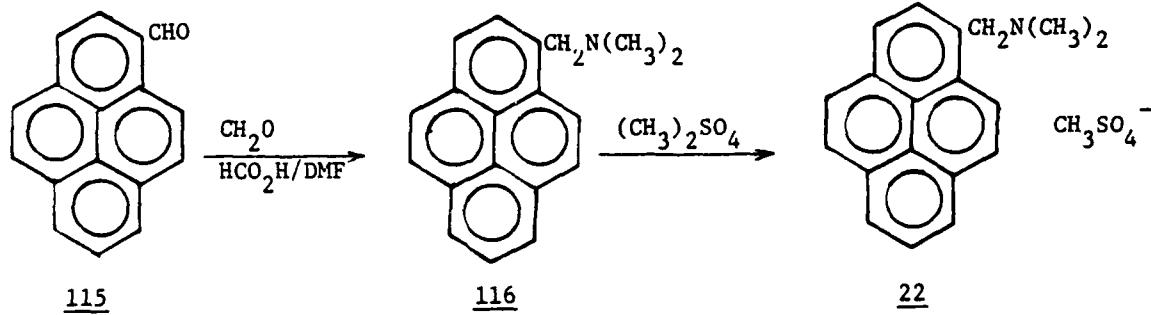


HPTS

However, its chemiluminescence was weak. Effort was begun on the preparation of cationic quaternary ammonium pyrene derivatives, all of which were readily prepared and easily purified.

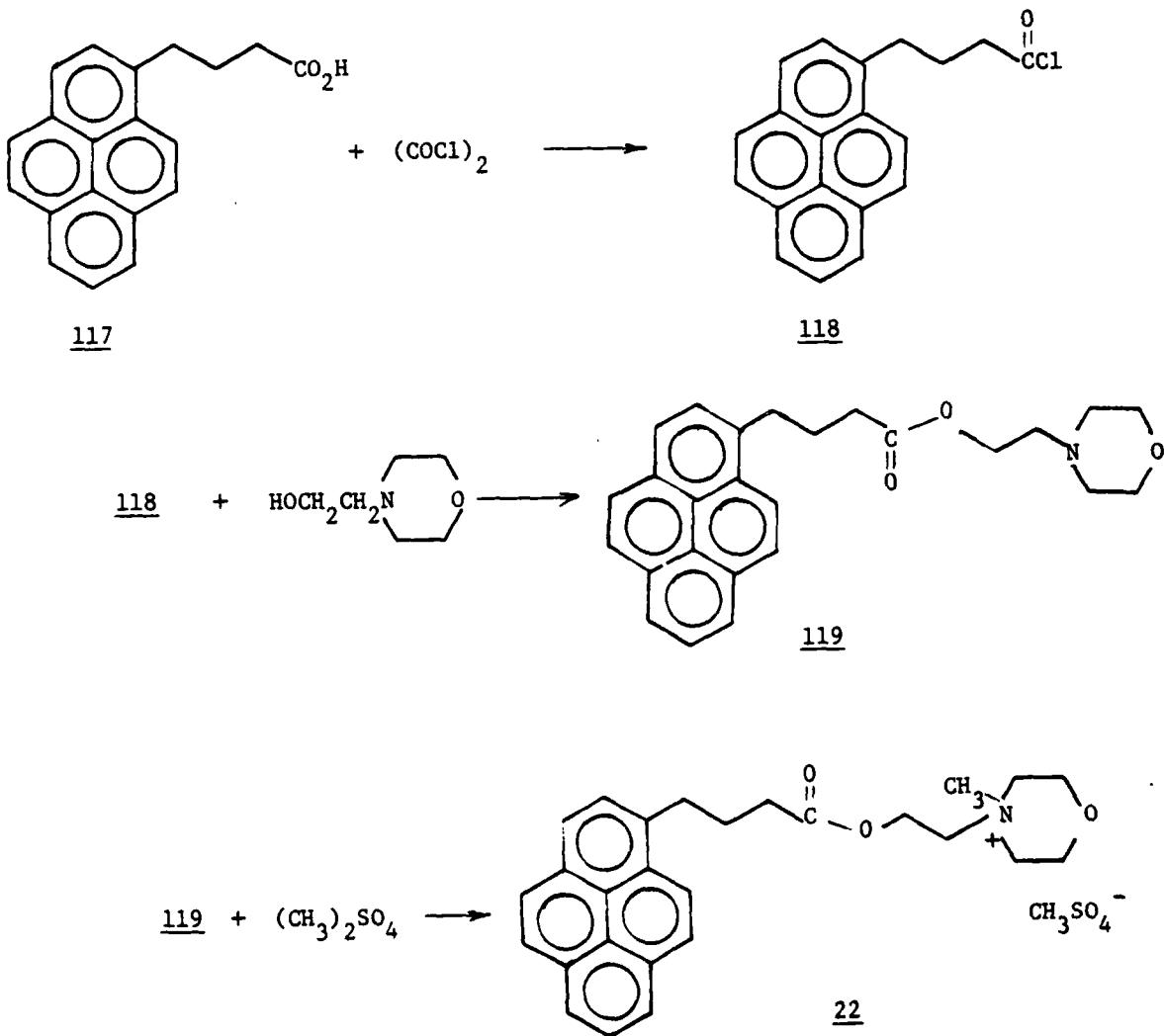
1-Pyrenecarboxaldehyde, 115, was heated with formic acid in DMF generating 1-pyrenylmethyldimethylamine, 116 (Scheme 22). The amine was quaternized with dimethylsulfate to 1-pyrenylmethyltrimethylammonium sulfate, 22. This fluorescer gave blue chemiluminescence in water and was slightly stronger than HPTS.

Scheme 22



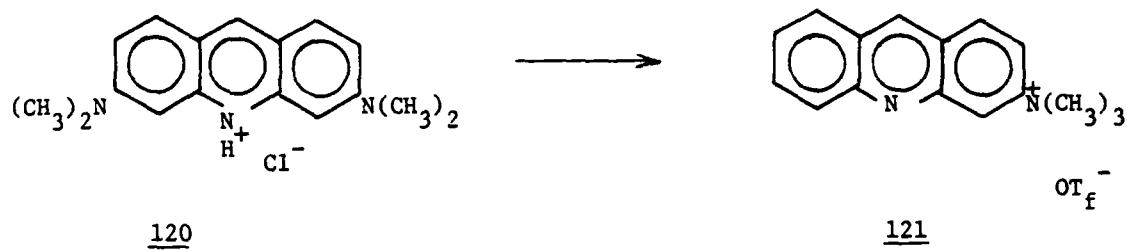
Scheme 23 illustrates the synthesis of another quaternary pyrene derivative. 1-Pyrenebutanoic acid, 117, was converted to its acid chloride with oxalyl chloride. The acid chloride, 118, was then esterified with hydroxyethylmorpholine to give 119. Quaternization with dimethylsulfate afforded the salt 21, which exhibited a much stronger chemiluminescence in water than HPTS or 22, possibly attributable to the longer insulation between the positive charge and the pyrene nucleus.

Scheme 23



Acridine Orange, 120, a commonly used cytochemical fluorescent dye available from Aldrich Chemical Co., was used to prepare the methylated quaternary ammonium salt, 121, as shown in Scheme 24. This fluorescer exhibited a weak orange chemiluminescence in water.

Scheme 24



B. OXALIC ACID DERIVATIVES: DESIGN AND SYNTHESIS

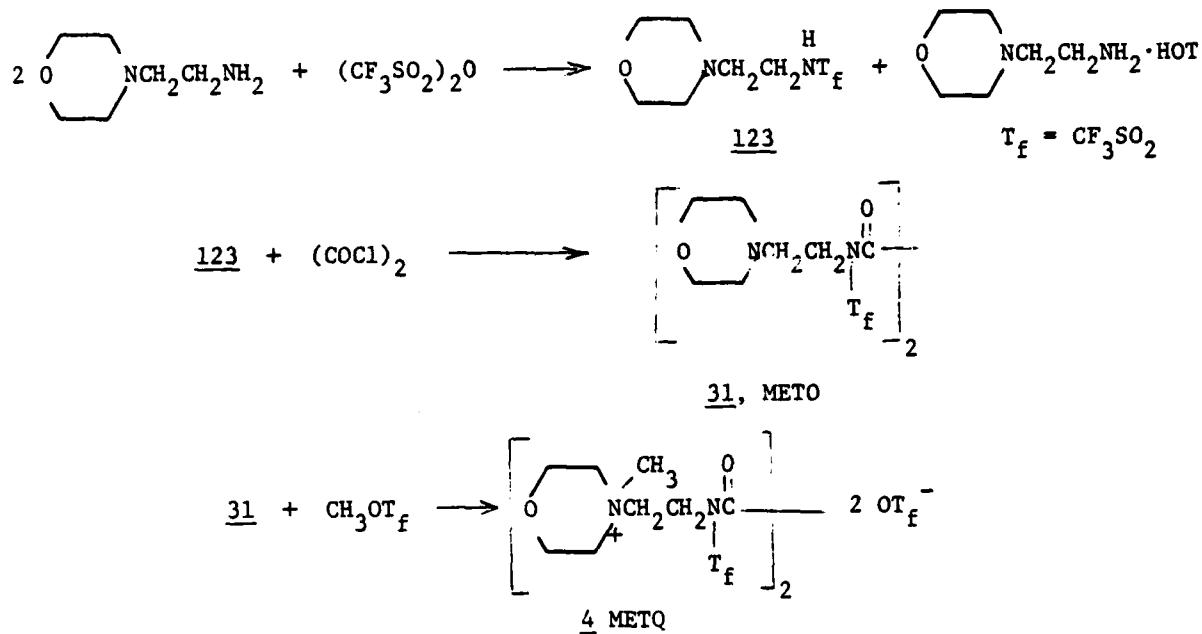
1. N-(TRIFLUOROMETHYLSULFONYL)OXAMIDES

A potential problem in the design of efficient oxalic acid derivatives for peroxyoxalate chemiluminescence in water is the fact that both water and hydrogen peroxide are nucleophiles. In principle, water could compete with hydrogen peroxide (probably as OOH ion) in the initial step of attack on the oxalate carbonyl group, leading to hydrolysis of the oxalic acid derivatives. It is generally known that oxamides are more stable than oxalate esters towards hydrolysis. However, previously synthesized chemiluminescent oxamides (32) only provided a maximum efficiency of 1%, which is substantially lower than the efficiencies obtained from the related oxalyl chloride (33), oxalic anhydride (34) and oxalate ester (13) chemiluminescent reactions. Recently, it was discovered in this laboratory that N-(trifluoromethylsulfonyl)oxamides or N-triflyloxamides, which contain the most powerful known electron withdrawing group, i.e. trifluoromethylsulfonyl (triflyl), provide efficient chemiluminescent reactions in peroxyoxalate systems (6,10). A series of N-triflyloxamides was prepared and their respective chemiluminescence efficiencies in an organic solvent, i.e. dibutylphthalate (DBP), were investigated. The results, summarized in Table 20, indicate that N-triflyloxamides which are further substituted on nitrogen by electronegative groups provide high chemiluminescence efficiency.

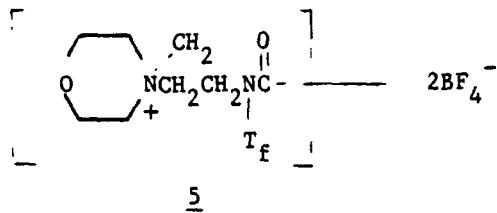
The discovery of this new, highly efficient class of N-triflyloxamides in peroxyoxalate chemiluminescence in non-aqueous media led to the synthetic studies directed towards optimizing the triflyloxamide structure to obtain maximum efficiency and solubility in an aqueous environment. The approach to a water-soluble N-triflyloxamide is to modify the structure by introducing water-solubilizing groups such as quaternary ammonium salts, polyoxyethylene chains, or sulfonic acid salts. A number of water-soluble N-triflyloxamides have been synthesized utilizing this approach.

The first water-soluble N-triflyloxamide prepared was METQ, 2. This compound was easily prepared by treating the amino substituted triflyloxamide (31, METO) with methyl trifluoromethanesulfonate in methylene chloride under dry conditions (Scheme 25). The product precipitated from the reaction medium and was isolated as a white crystalline solid. The product (mp 160-165) gave a satisfactory elemental analysis. It could be recrystallized from isopropanol-acetonitrile, but the recovery was less than 50% of the original material.

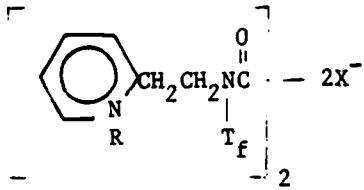
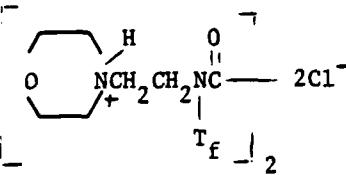
Scheme 25



In the preparation of triflylamide 123, an additional molar equivalent of N-(2-aminoethyl)morpholine was used to replace triethylamine as the acid acceptor, since it gave a cleaner product. The tetrafluoroborate salt, 5, (mp 198-204) was similarly prepared by quaternization of METO with trimethyloxonium tetrafluoroborate in methylene chloride. Reaction of METO with dimethyl sulfate gave a gummy product, and attempts to prepare the methylmorpholinium iodide or chloride of METO were also unsuccessful.

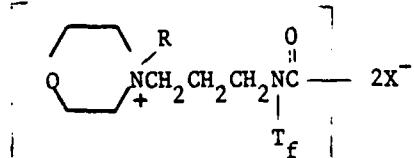
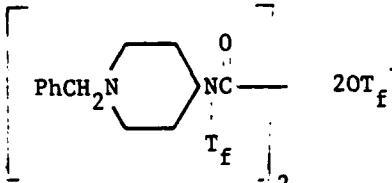


A pyridinium quaternary ammonium salt (1, PETQ) was prepared from bis[2(2-pyridyl)ethyl]-N,N'-bis(trifluoromethylsulfonyl)oxamide which was prepared from the N-[2-(2-pyridyl)ethyl]trifluoromethane sulfonamide precursor according to the procedure outlined in Scheme 25. The hydrochloride salt (124, METH) was obtained by treatment of METO with hydrogen chloride gas in tetrahydrofuran (THF) at room temperature. It was also isolated as the minor product in the oxalation of METO (Scheme 25).

1, PETQ: R = CH₃, X = OT_f2, PETH: R = H, X = Cl

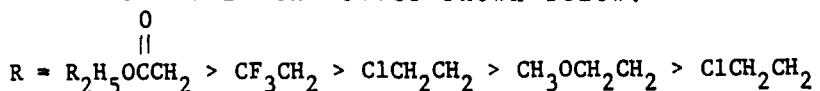
METH

A related pyridine derivative, 2 (PETH), on the other hand, was unexpectedly obtained in good yield during the oxalation of the corresponding triflylamide in THF in the presence of 4-dimethylaminopyridine. Both METH (124) and PETH were recrystallized from acetonitrile and confirmed by elemental analysis and spectral data. Other water-soluble triflyloxamides such as 125, 6, and 9, related to METQ, were also prepared by a similar procedure. Details are described in the Experimental Section.

6, MPTQ: R = CH₃, X = OT_f125, R = H, X = Cl

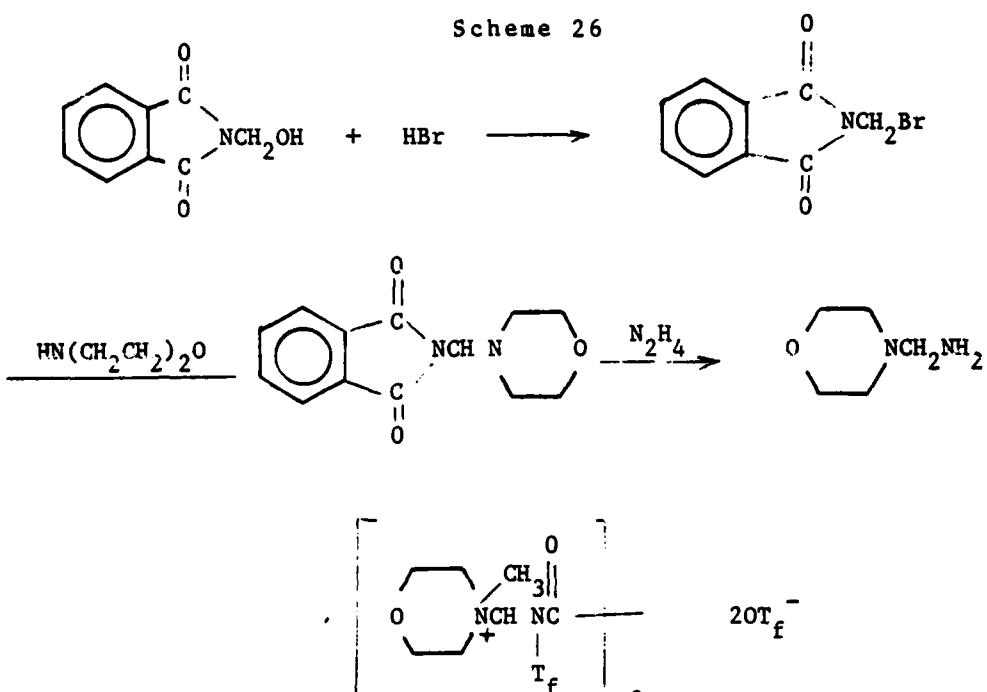
BPTQ

The chemiluminescence performance of N-triflyloxamides in dibutyl phthalate (Table 20) shows that in the alkyl amine series the efficiencies are in the order shown below:

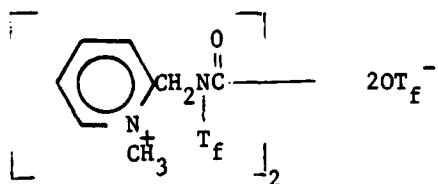


This suggests that N-triflyloxamides with an electronegative water-solubilizing group substituted on the methylene carbon may be more efficient than METQ in the aqueous chemiluminescent system. Thus, the initial approach was an attempt to synthesize aminomethylmorpholine (Scheme 26), the starting compound for the preparation of MMTQ, (126), a homolog of METQ.

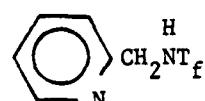
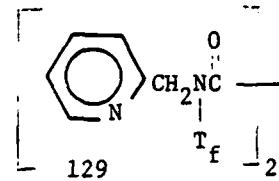
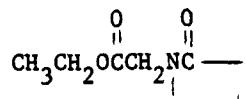
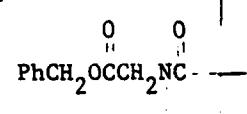
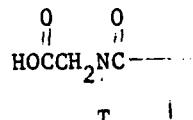
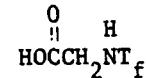
Scheme 26

126, MMTQ

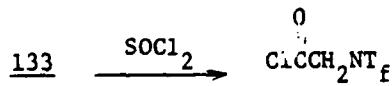
Reaction of N-(hydroxymethyl)phthalimide with HBr in concentrated sulfuric acid at 75 C. readily gave N-(bromomethyl)phthalimide. Treatment of this intermediate with morpholine in dioxane at room temperature afforded N-(morpholinomethyl)phthalimide as a white solid product (mp 98-100) whose structure was confirmed by NMR and by elemental analysis. However, attempts to remove the amino-protecting phthaloyl group by hydrazine hydrate resulted in a mixture of products, and separation of the desired amine proved to be very difficult. The second compound of choice was PMTQ, (127), a homolog of PETQ.,

129, PMTQ

Triflylamide 128 was readily prepared from the commercially available 2-aminomethylpyridine. Problems arose in attempting to convert this compound to the triflyloxamide 129. Only trace amounts of 129 were isolated when 128 was treated with oxalyl chloride in the usual manner. The major product appeared to be polymeric. The presence of the HCl acceptor triethylamine may have promoted the polymerization of 128. More careful manipulation of the reaction conditions may give 129 in a useable quantity.

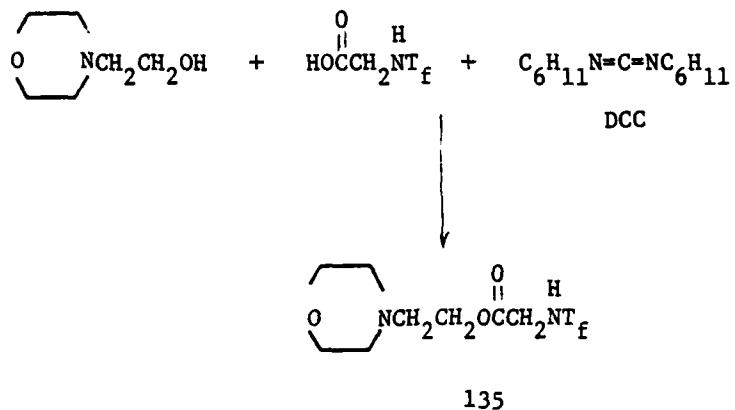
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The high chemiluminescent efficiency (12.8%, Table 20) of the ester 130 prompted the synthesis of the corresponding benzyl ester, 131. As expected, compound 131 gave strong chemiluminescence in the phthalate solvent with a quantum yield of 10.0%. The advantage of the benzyl ester over the ethyl ester is that the benzyl group can be reductively removed by catalytic hydrogenolysis rather than by acid-catalyzed hydrolysis. The resulting carboxylic acid, 132, had the potential for water-solubility as well as for being a valuable intermediate for the synthesis of other water-soluble derivatives such as salts. However, treatment of 131 with hydrogen over 10% Pd/C gave a quantitative conversion to the triflylamide 133 instead of the desired compound 132. Apparently both the benzylic and oxalyl groups were cleaved under these conditions. Compound 133 was also readily prepared by hydrolysis of the ethyl ester 130 in dilute HCl. Treatment of 133 with excess thionyl chloride afforded the corresponding acid chloride, (117), in good yield.

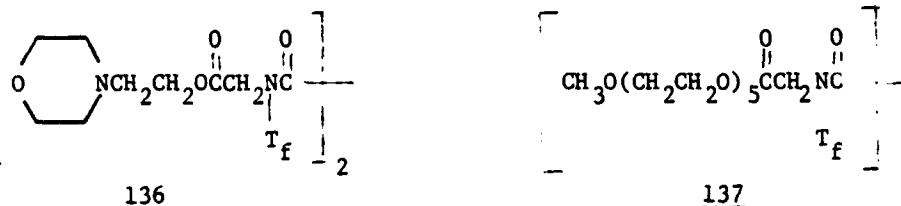
134

Attempts were now made to introduce water-solubilizing groups into the oxamide. It was discovered that the use of N,N'-dicyclohexylcarbodiimide (DCC) as a esterification reagent along with 4-pyrrolidinopyridine as a catalyst (34) was an effective method for synthesis of esters of 133 without production of an acidic by-product. Scheme 27 illustrates this method for the synthesis of the morpholinoethyl ester 135.

Scheme 27



Compound 135 could then, in principle, be converted to the oxamide 136 and quaternized to a water-soluble product. Unfortunately, several attempts to convert 135 to the oxamide failed to give a clean product.



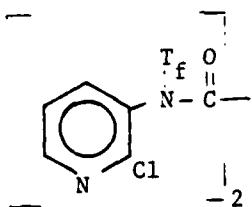
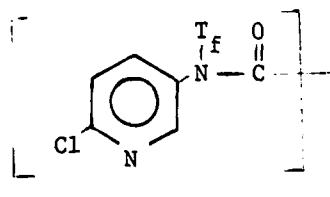
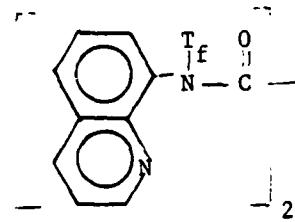
Similar results were obtained in the attempted synthesis of the polyoxyethylene-substituted triflyloxamide, 137.

The successful synthesis of N-triflylglycine esters was extended to amides. Thus, the reaction of the acid chloride 134 with two molar equivalents of N-methylpiperidine afforded the triflylamide (138), which upon oxalation gave a chemiluminescent product.

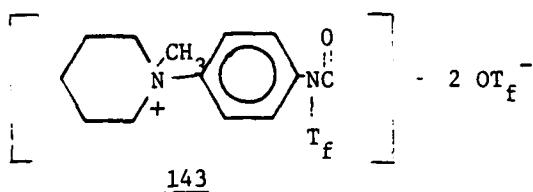


The infrared spectrum of this product suggested that the desired triflyloxamide 139 was present along with salts. Attempts to purify 139 have thus far been unsuccessful. However, further efforts should be made to obtain this oxamide in a pure state for quantitative evaluation of its performance in the aqueous chemiluminescent reaction.

The high efficiency of the pyridyl-substituted oxamide 140 in dibutyl phthalate also led to an attempt to quaternize this compound with methyl triflate. Examination of the product mixture by infrared spectroscopy indicated that the oxamide carbonyl bands at 1750 and 1730 cm⁻¹ had disappeared, and the product was not chemiluminescent. Similar results were obtained in the attempted quaternization of triflyloxamides 141 and 142.

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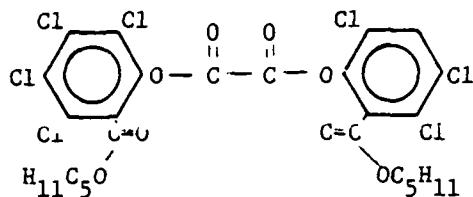
This series of heteroaromatic triflyloxamides is apparently too reactive towards N-alkylation. A less reactive phenyl-substituted quaternary ammonium triflyloxamide, 143, was prepared from the commercially available p-morpholinoaniline.

143

This compound gave only a weak chemiluminescence in the aqueous reaction. Additional electron-attracting groups such as chlorines substituted on the phenyl ring may be required for efficient chemiluminescence in water. Future research should be focused on this class of compounds.

2. CHLOROPHENYL OXALATE ESTERS

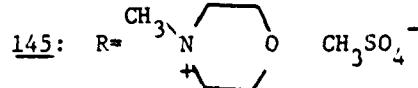
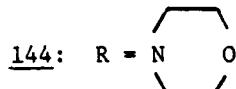
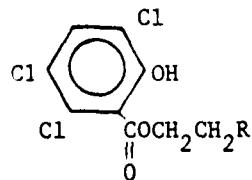
The oxalate ester CPPO is currently employed in the non-aqueous chemical light system used in the Cyalume lightstick. This compound has the highest light capacity of any oxalic acid derivative (900 lumen hr per liter) and is highly efficient in dibutyl phthalate (QY 17%) (8).



CPPO

Introduction of a side chain containing a quaternary ammonium or polyoxyethylene group might be expected to provide water-solubility while maintaining the efficiency of the balance of the structure.

Previous attempts to introduce an amino side chain into 3,5,6-trichlorosalicylic acid via the usual acid chloride route had failed due to lactide formation (11). Use of the DCC method avoided this difficulty and readily afforded the amino-substituted ester 144. This white crystalline solid was purified by preparative HPLC and its structure confirmed by spectroscopic evidence and elemental analysis. Treatment of 144 with oxalyl chloride failed to yield the desired oxalate ester, 146. The infrared spectrum of the crude product indicated the presence of carbonyl groups with absorptions at 1770 and 1730 cm⁻¹, too low for oxalate ester carbonyl groups. As an alternate route, the morpholino nitrogen of the phenol was quaternized first with dimethyl sulfate to give the pure salt 145. Oxalation of this salt gave a mixture of hygroscopic chemiluminescent products which resisted purification. In future attempts quaternization should be carried out with methyl triflate or methyl chloride to avoid this problem. These salts tend to be less hygroscopic than the methyl sulfate salts. The methyl chloride quaternary has the additional advantage of the chloride anion, the same one produced in the oxalation step.



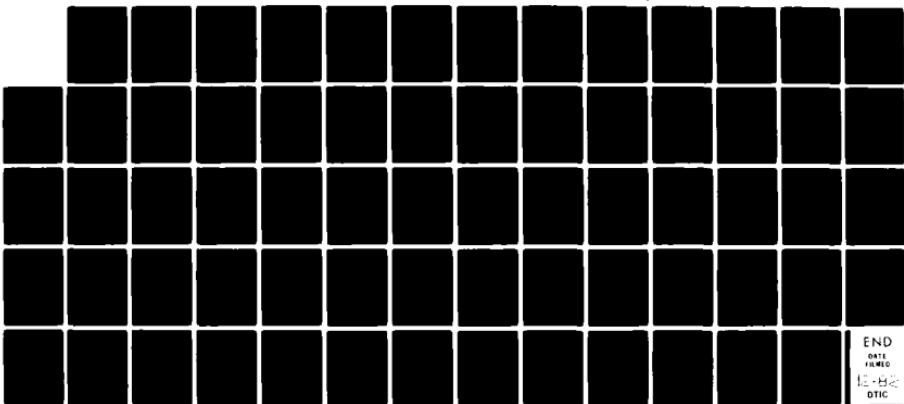
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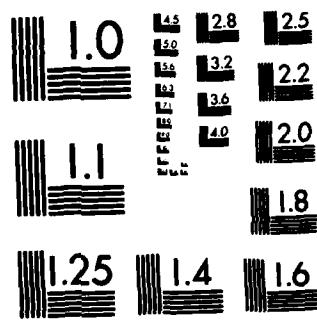
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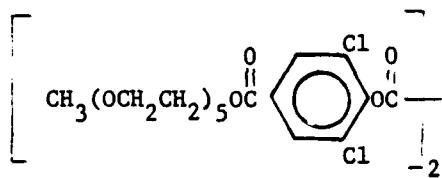
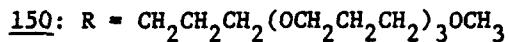
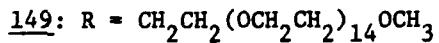
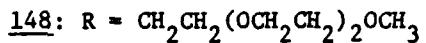
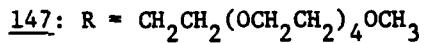
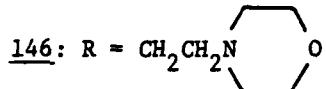
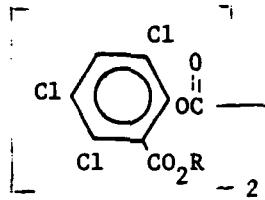


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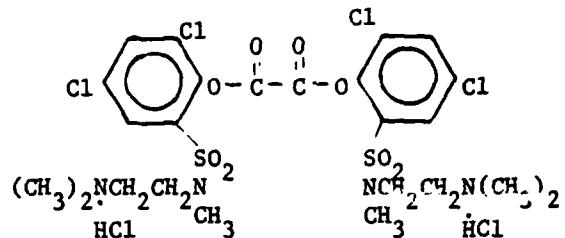
Direct esterification of 3,5,6-trichlorosalicylic acid with polyoxy alcohols was also achieved by the DCC method or by the standard direct esterification with p-toluenesulfonic acid as catalyst in xylene solvent. These esters were easily purified by preparative scale HPLC. Oxalation of these phenols in THF by the usual method with triethylamine gave the expected oxalate esters 147, 148, 149, and 150. For comparison, oxalate ester 151 was prepared to determine whether substituting the solubilizing function on the para position of the phenyl ring had any effect on performance.



151

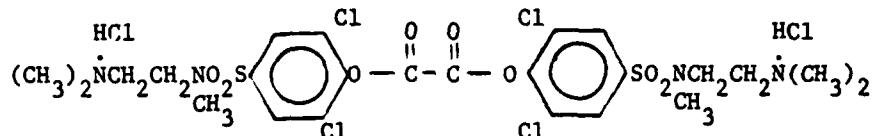
These compounds were usually isolated from the reaction mixture in a fairly pure state. Further attempts to purify these products by preparative HPLC resulted in contamination and loss of material, probably because of decomposition on the column. Although these polyoxy analogs of CPPO give moderate chemiluminescence in water, they are liquids, and purification is accordingly very difficult.

As described in Section 2 of this report, the feasibility of aqueous peroxyoxalate chemiluminescence was first demonstrated in these laboratories in an earlier program (11). The most efficient oxalate ester prepared in that program was SAPO.



SAPO

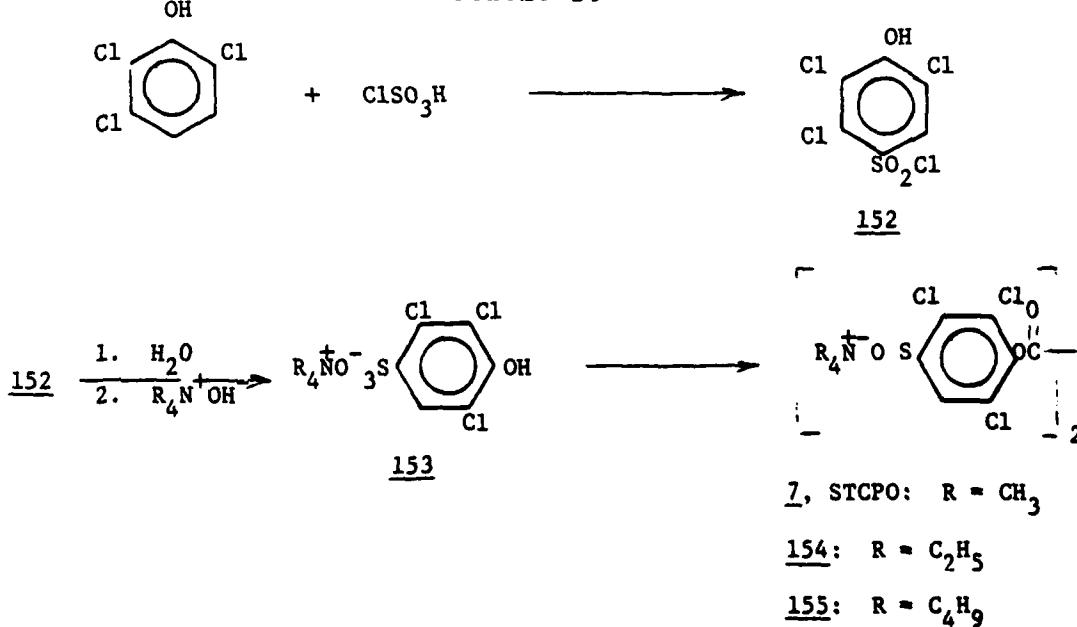
The low solubility of SAPO in water limited the potential of this compound for high light output. A related compound, PAPO, was also prepared and found to give bright, but short-lived chemiluminescence in water. The short lifetime may have been limited by the rapid hydrolysis of PAPO in water (11).



PAPO

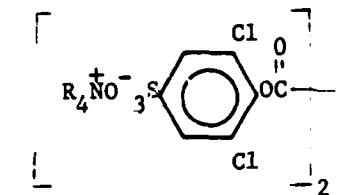
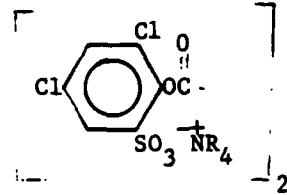
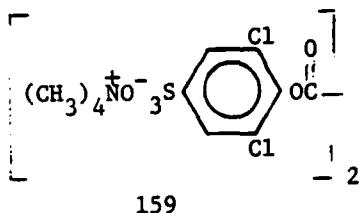
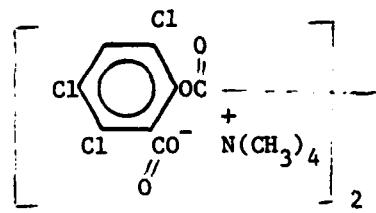
Attention was therefore shifted to the synthesis of water-soluble oxalate esters derived from tetra-alkylammonium salts of 2,3,4-trichloro-4-hydroxybenzenesulfonic acid. The general synthetic route to these compounds is outlined in Scheme 28.

Scheme 28



Compounds 7 (STCPO), 154, and 155 were obtained as solids, and their structures were confirmed by IR, NMR, and elemental analysis. Since the oxalation by-product, triethylamine hydrochloride, and the oxalate esters 154 and 155 had similar solubility, 3A molecular sieves were used instead of triethylamine as the acid scavenger. The sieves could then be filtered from the product mixture, and the product isolation was much simpler. This new process (10) was also effective in the preparation of triflylamides and triflyloxamides.

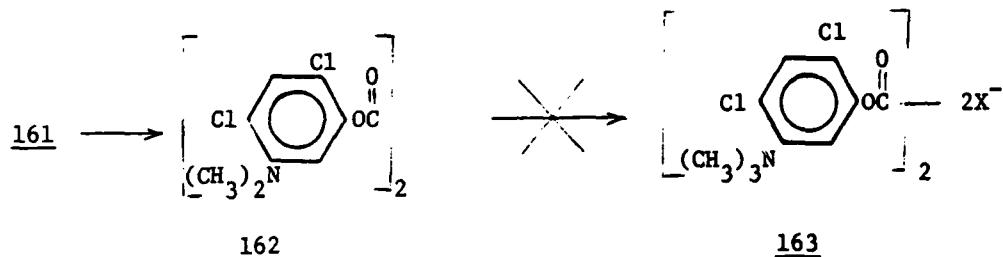
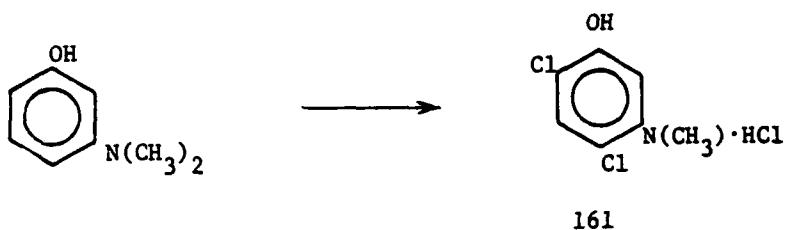
The sulfonic acid salt STCPO is highly soluble in water and gives bright but short-lived chemiluminescence in aqueous solution. Compounds 154 and 155 are less soluble in water than STCPO, but their chemiluminescent lifetimes are longer. Several other less reactive members of this class, oxalate esters 156 through 159, were prepared in a similar manner.

156: R = CH₃157: R = C₄H₉158: R = CH₃159160

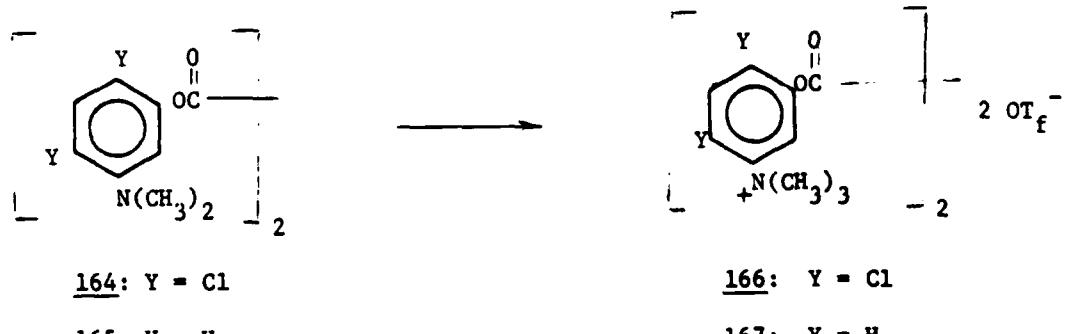
For comparison, the tetramethylammonium salt of 2,3,5-trichlorosalicylic acid was prepared and converted to the oxalate ester, 160. All of these showed bright but short-lived chemiluminescence in water.

Substitution of a quaternary ammonium group directly on the aromatic ring of an aryl oxalate was expected to enhance the reactivity, since this group is a strong electron-attractor. Thus, the oxalate ester 162 was prepared according to the sequence outlined in Scheme 29.

Scheme 29

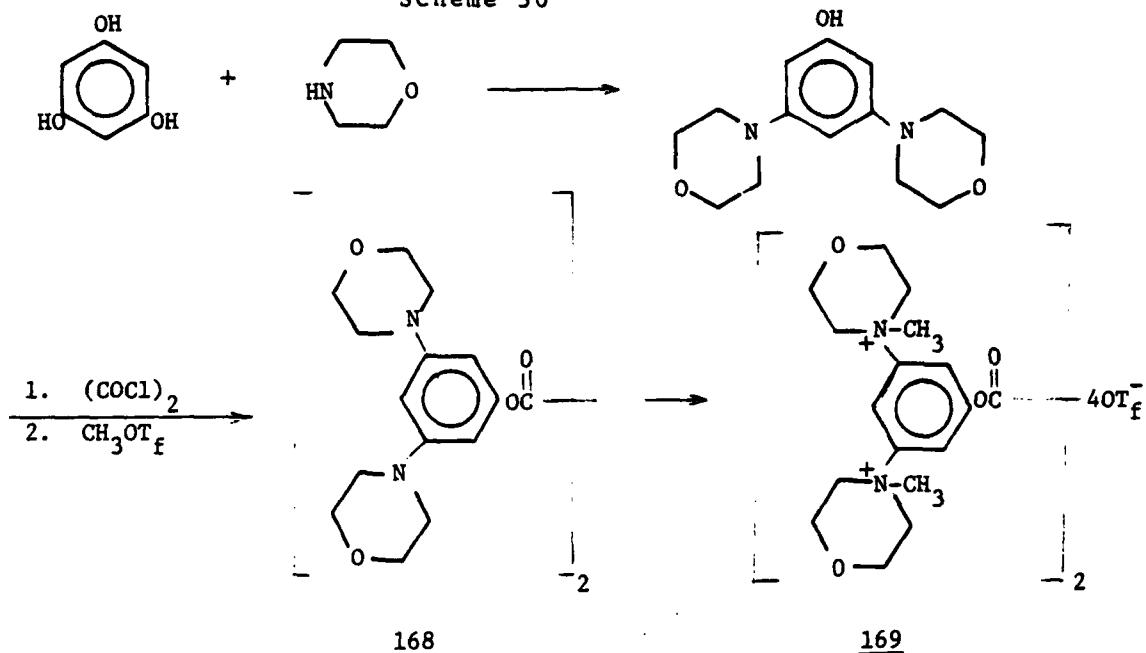


Analytically pure 162 was obtained by recrystallization of the crude product from acetonitrile. It gives efficient chemiluminescence in dibutyl phthalate with a quantum yield of 3%. Attempted quaternization of 162 with either dimethyl sulfate or methyl triflate gave only recovered starting material in addition to a non-chemiluminescent minor by-product. Presumably, the presence of the three electron-attracting chlorines and the oxalate ester itself decreases the electron density on the amino nitrogen to a point where quaternization does not occur. The fact that both the dichloro and the non-chlorinated oxalate esters, 164 and 165, readily quaternize to the respective salts, 166 and 167, tends to support this hypothesis.



Synthesis of a diaminophenyl oxalate such as 168 was accomplished via the condensation of phloroglucinol with morpholine in an autoclave followed by oxalation of the diamine in the usual manner (Scheme 30).

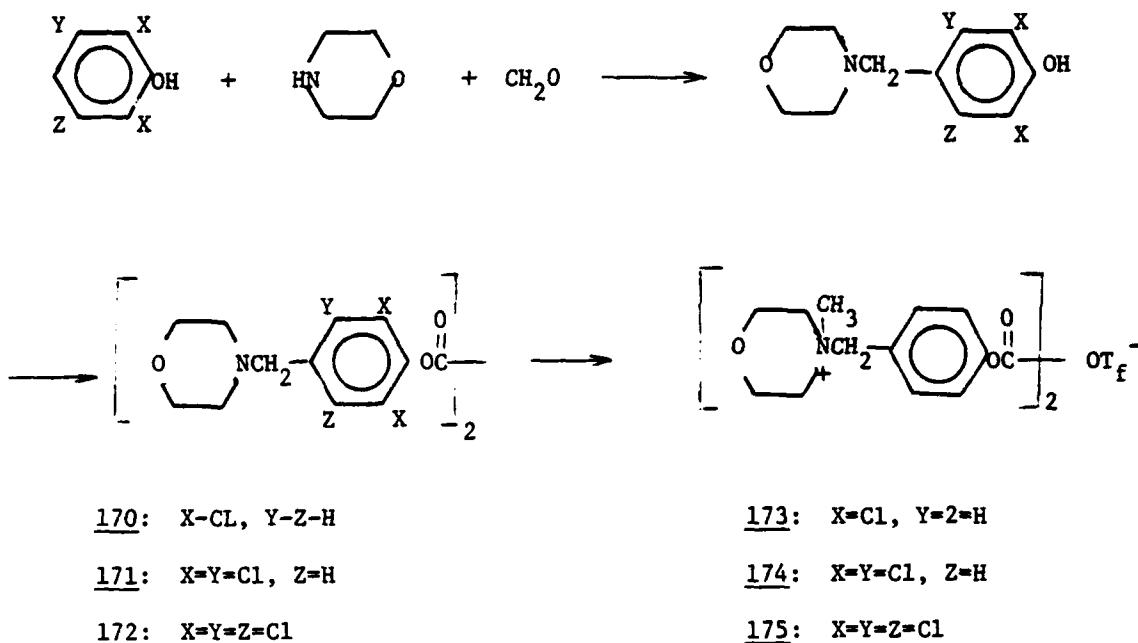
Scheme 30

168169

Treatment of the oxalate ester 168 with methyl triflate afforded the quaternary ammonium salt 169. All of the quaternary ammonium salts 166, 167 and 169 are highly soluble in water but give only moderate and short-lived chemiluminescence in water. It seemed reasonable that these compounds might be too reactive, with rapid hydrolysis competing with the perhydrolysis in the aqueous media. One might expect that the initial hydrolysis product, presumably a half-oxalate ester, would be a strong quencher of the chemiluminescent reaction. It is well known that oxalic acid strongly inhibits the peroxyoxalate chemiluminescent reaction in non-aqueous media (9).

Based on these observations a new series of oxalate esters was prepared where a methylene group was positioned between the amino function and the phenyl ring. This was expected to insulate the quaternary ammonium group and substantially reduce the electron withdrawing effect. The aminophenols were readily prepared via the Mannich reaction of the appropriate chlorophenols with morpholine and formaldehyde as outlined in Scheme 31.

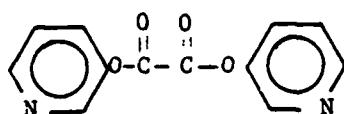
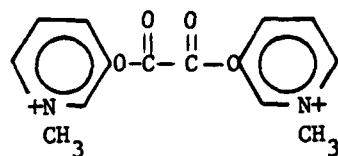
Scheme 31



The product yields in the Mannich step, after recrystallization, ranged from 50% to 80%. The oxalations and quaternizations were carried out in the usual manner. All of the oxalate esters prepared gave weak to moderate chemiluminescence in dibutyl phthalate, and the quaternized products gave weak to moderate chemiluminescence in water.

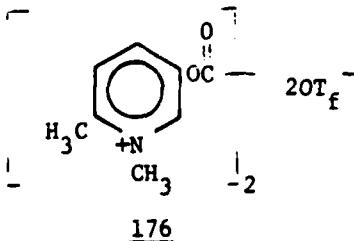
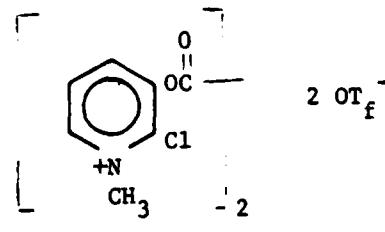
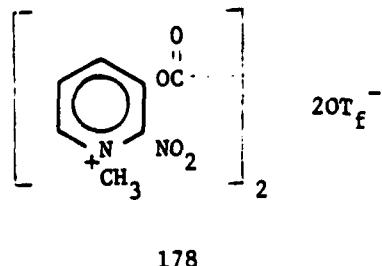
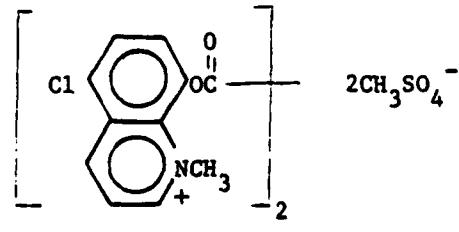
3. PYRIDYL AND QUINOLYL OXALATE ESTERS

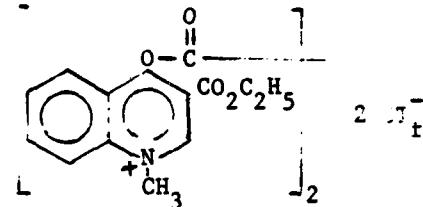
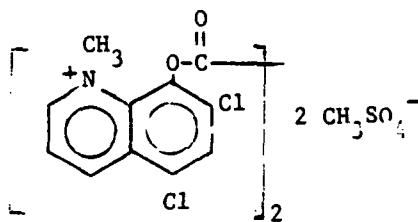
It was shown in an earlier study (13) that the reaction of oxalyl chloride with 2-hydroxypyridine yielded the oxamide derived from 2-pyridone (35) rather than the expected oxalate ester, 36. Chemiluminescence was observed from the reaction of 35 with acid catalysis. Apparently the product was derived from tautomerization of 2-hydroxypyridine in the presence of oxalyl chloride. The possibility of tautomerization does not exist with 3-hydroxypyridine so that treatment of this isomer with oxalyl chloride in the presence of triethylamine gives the expected ester, 37. The oxalate ester 37 gave a strong but short-lived chemiluminescent reaction in the phthalate solvent system.

3738

Quaternization of 37 afforded the bis-quaternary ammonium salt, 38, which gave substantial chemiluminescence in dibutyl phthalate but was not chemiluminescent in water. Infrared and NMR studies indicated that 38 underwent rapid hydrolysis in water within 5 minutes of mixing. A number of other pyridyl and quinolyl oxalate esters were prepared, and their performance in dibutyl phthalate is summarized in Table 21.

Quaternization of the respective oxalate esters with methyl triflate or dimethyl sulfate gave the corresponding water-soluble salts (176 through 181).

176177178179

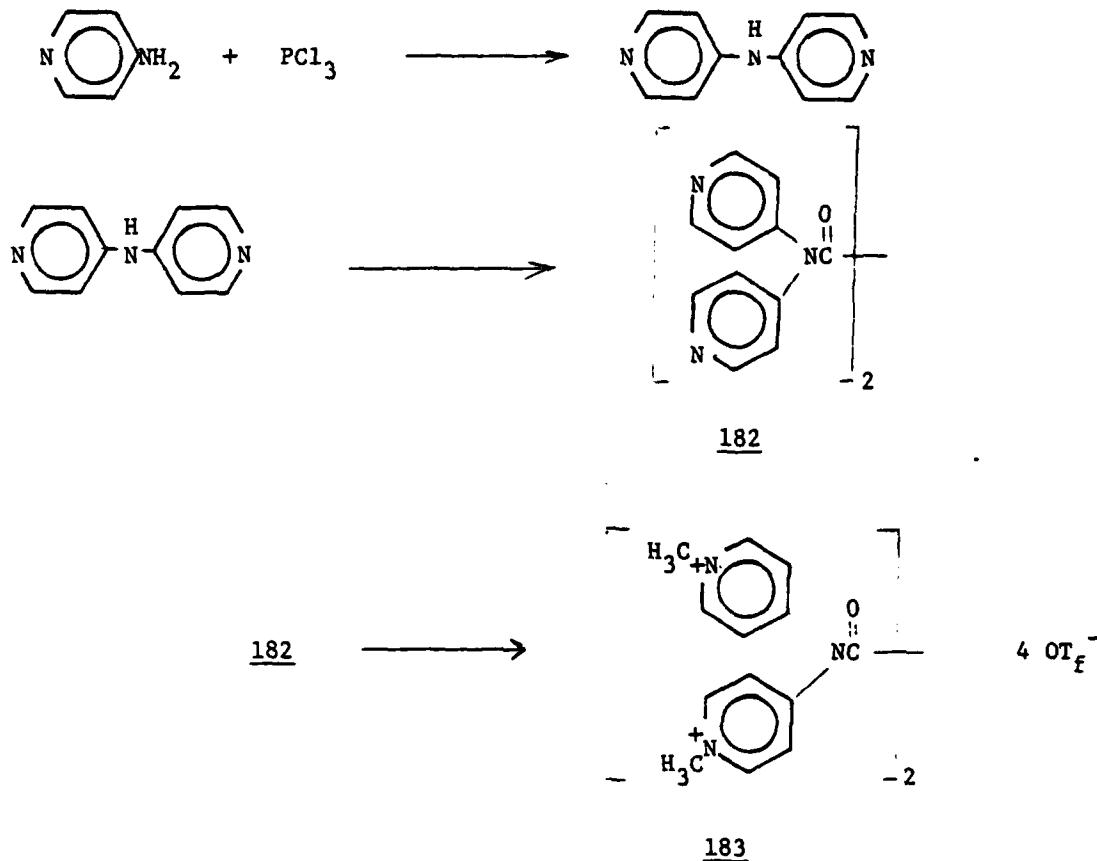


In general, all of these salts, with the exception of 181, have good water-solubility. The chemiluminescence performance of these materials in water was not comparable to the triflyloxamides or to the chlorophenyl oxalate esters. The exceptions were 177 and 181, which provided moderate chemiluminescence in the surfactant-enhanced aqueous system. Perhaps further studies of the structural effects in this series could lead to improvement of the efficiency of this new class of oxalic acid derivatives.

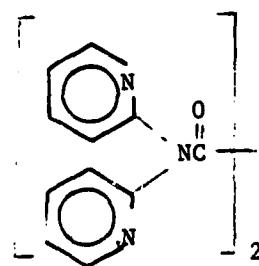
4. MISCELLANEOUS WATER-SOLUBLE OXALIC ACID DERIVATIVES

Other new classes of water-soluble oxalic acid derivatives were investigated. Several oxamides were prepared in which electron-attracting groups were substituted on the nitrogen atom. A novel oxamide, 183, was prepared as outlined in Scheme 32.

Scheme 32

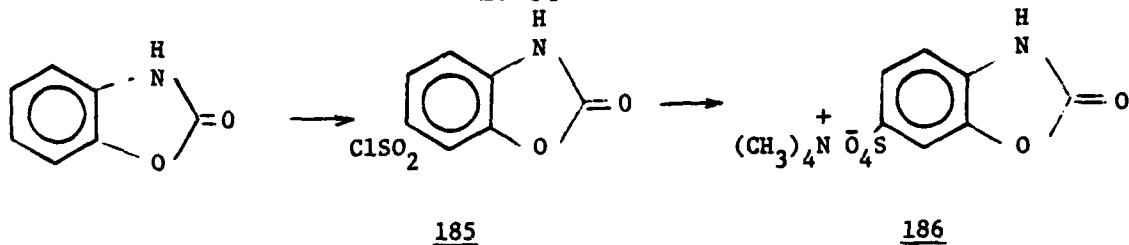
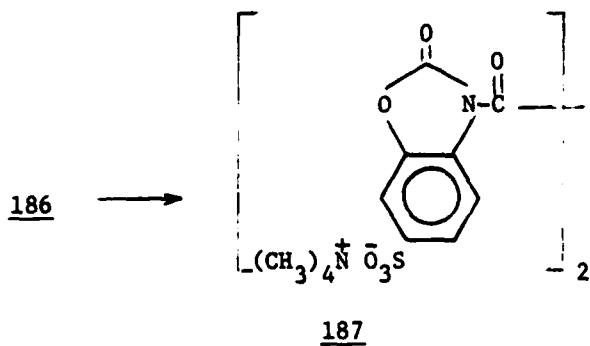


4,4'-Dipyridylamine was prepared in 65% yield from 4-aminopyridine according to a procedure described in the literature (35). The corresponding oxamide, 182, and quaternary salt, 183, were prepared by the usual routes. The salt 183 was very soluble in water and gave bright but short-lived emission in the aqueous chemiluminescent reaction. An analog, 184, was prepared, but several attempts to quaternize this amine were unsuccessful.

184

Another synthetic approach to water-soluble oxamides is the introduction of the water-solubilizing group prior to the oxalation step. An example of this method is outlined in Scheme 33.

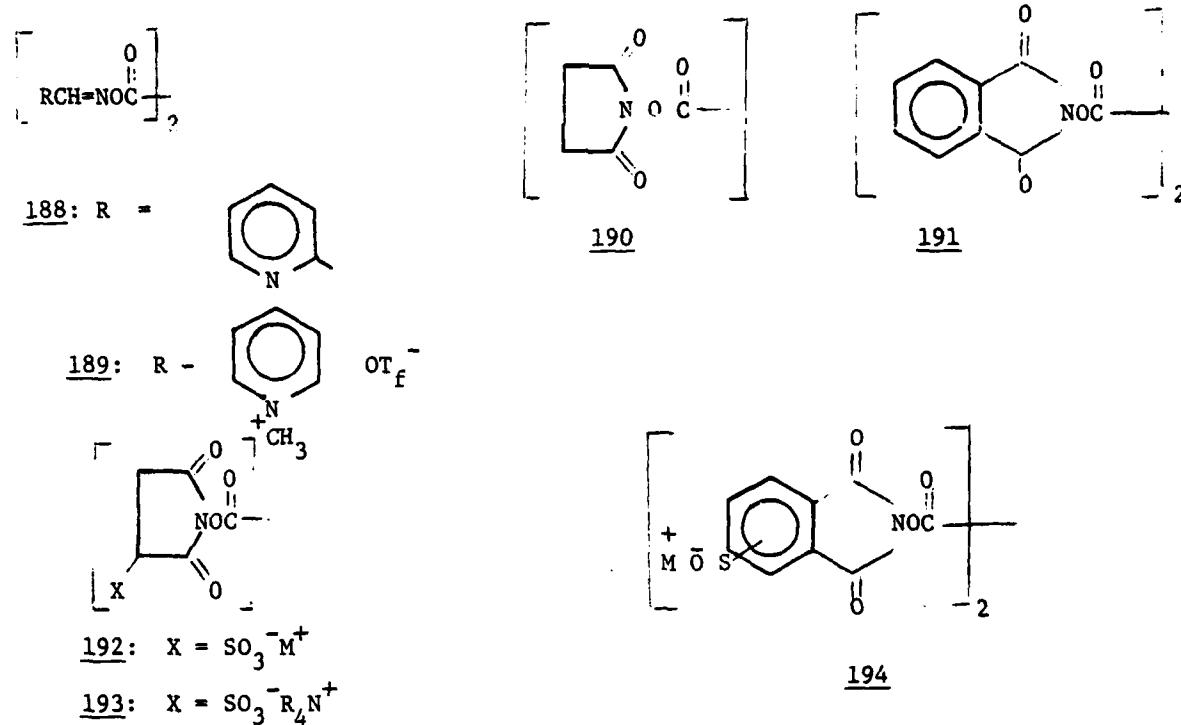
Scheme 33

185186187

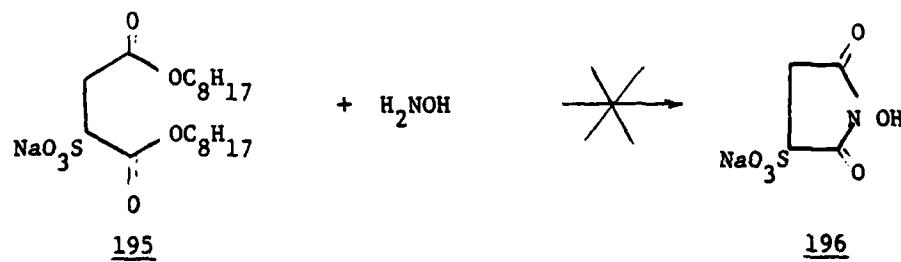
Chlorosulfonation of 2-benzoxazolinone was achieved by the known procedure (36). The desired oxamide was obtained as a white crystalline solid, 187. This compound was highly soluble in water, but gave only weak, short-lived emission in water. It appeared that rapid hydrolysis was responsible for the poor performance. The same approach, introducing water-solubility prior to the final oxalation step, was used in the preparation of oxalate esters 7,154-160, 179 and 180.

Presumably due to poor solubility in all solvents examined, the oxalate ester 188 failed to give a chemiluminescent reaction. Quaternization of 188 afforded the expected salt, 189, which was moderately active in dibutyl phthalate but inactive in water.

Oxalation of N-hydroxysuccinimide and N-hydroxyphthalimide gave the expected esters, 190 and 191. Both gave strong chemiluminescence in phthalate solvent and weak to moderate activity in water even though aqueous solubility was poor. These results suggested that introduction of water solubility into these substrates might yield compounds active in water. Attempts were therefore made to synthesize compounds 192, 193, and 194.



Reaction of sodium dioctylsulfosuccinate, 195, a commercially available surfactant, with hydroxylamine in 2-methoxyethyl ether or dimethylformamide at reflux yielded a mixture of products which was separated by column chromatography. NMR spectra indicated that none of these products was the desired succinimide, 196, precursor for the oxalate ester, 192. Chlorosulfonation of N-hydroxyphthalimide, followed by hydrolysis, resulted in the formation of phthalic acid rather than the desired N-hydroxysulfonylphthalimide, the intermediate for 194. Several other attempts to prepare this intermediate were also unsuccessful.



EXPERIMENTAL SECTION

Instrumentation

Melting points were taken on a "Mel-Temp" block and are uncorrected. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer; samples were run in Nujol or in methylene chloride solutions. All IR values in this section are reported in cm⁻¹. NMR spectra were recorded on a Varian Associates Model EM360A spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded on a VG Micromass Model 7070F high-resolution mass spectrometer attached to a VG Model 2035 data system, using the electron impact (EI) mode or the chemical ionization (CI) mode. In the CI mode, methane was used as the reagent gas. Preparative HPLC was run using a Waters Associates Prep 500A chromatograph, employing either silica or reverse-phase C18 silica pre-packed columns; the detector was either an Altech absorption detector or the integral refractive index detector of the instrument. Gas chromatography was carried out on a Hewlett-Packard Model 5840A gas chromatograph using 6 ft., 1/8 inch glass columns containing 10% OV-17 as the mobile support. Thin layer chromatography (TLC) was carried out using either Whatman LK5DF silica gel or Whatman KC18DF reverse-phase C18 silica gel. Microanalyses were performed by the Micro Analytical Laboratories of American Cyanamid Company, Bound Brook, N.J. Kinetic studies of fluorescer decomposition were carried out on a Hewlett Packard 8450A UV/VIS spectrophotometer, and statistical data analysis was accomplished via the MINITAB program on a DECSYSTEM-10 computer.

Chemiluminescence Quantum Yields

Absolute light measurements were made on a spectroradiometer-luminometer, similar to that described by Roberts and Hirt (37), modified with a Jarrell-Ash Model 82-410 grating monochromator and an RCA C31034 photomultiplier with a gallium arsenide photocathode operated at 1300V with dry ice cooling in a housing from Products for Research Inc. (model TE-241-RF). Raw data were recorded digitally on a Hewlett-Packard 5150A thermal printer. Spectral response was corrected by calibration against a standard tungsten lamp (traceable to the N.B.S.). Absolute light intensities were obtained by deriving calibration constants based on the accepted fluorescence quantum yield (0.55) for quinine sulfate (38) in 0.1 N sulfuric acid and by ferrioxalate actinometry (39) of the exciting light. Chemiluminescence quantum yields in einsteins per mole of ester or oxamide were calculated by monitoring the intensity decay at a single wavelength and calculating the intensity at each time interval in the appropriate units from the chemiluminescence spectrum. Chemiluminescence spectra were corrected for intensity decay. The total area under the decay curve was calculated by using a combination of a Simpson's rule integration and an exponential extrapolation to infinite time (37). Data were processed via a Digital Equipment Corp. PDP-1140 computer.

p-n-Octylphenylacetylene (91a)

A stirred solution of n-octylbenzene (150 g; 0.79 mole), ethylene dichloride (300 ml), and acetyl chloride (62.04 g; 0.79 mole) was cooled to 0-5 C. and charged with aluminum chloride (115.8 g; 0.87 mole) during 1.5 hr, while keeping the temperature below 10 C. The mixture was slowly warmed to room temperature and stirred for 96 hr. It was then quenched on an ice-HCl mixture, heated to 90 C., and stirred. The reaction mixture was then stirred in an ice bath at 10-15 C., at which time a low melting solid precipitated. This solid was quickly filtered and then taken up in ether and washed twice with 100 ml of water and some brine. The ether layer was dried over magnesium sulfate, filtered, and the filtrate evaporated under reduced pressure, leaving a red oil, wt. 233.5 g. Distillation of this oil afforded a major fraction having bp 147-152 @ 0.5 mm, wt. 182.4 g. GC and NMR indicated this fraction to be 98% p-n-octylacetophenone. The acetophenone (174.8 g; 0.75 mole) was charged slowly with phosphorus pentachloride (166 g; 0.8 mole) at room temperature and stirred. After 5-10 min an exotherm began, and the reaction mixture was cooled in an ice bath and stirred for 1 hr. Removal of phosphorus oxychloride under reduced pressure left an oil which was shown by GC to be free of any starting material and to consist of an 87% mixture of the two chlorinated products. The chlorinated product mixture, 212 g, was charged with 700 ml of ethanol and 198 g of 85% KOH. After refluxing 1 hr, GC showed only 14% product. An additional 100 g of KOH was added and the mixture refluxed for 42 hr. At this point, GC showed 60% product formation. The reaction mixture was drowned in water, and ether was added. The ether layer was washed with water and then with dilute acetic acid until neutral. It was dried over magnesium sulfate, filtered, and evaporated under reduced pressure, leaving 242 g of crude oil. Distillation afforded 67 g of a major fraction having a bp 128 C. @ 0.8 mm. This fraction was identified by GC and NMR as being 90% p-n-octylphenylacetylene.

p-n-Dodecylphenylacetylene (91b)

A stirred solution of n-dodecylbenzene (150 g; 0.6087 mole), acetyl chloride (43.5 ml; 0.6087 mole), and ethylene dichloride (300 ml) was cooled to 0-5 C. and charged with aluminum chloride (89.38 g) during 1.5 hr, while keeping the temperature below 10 C. The mixture was slowly warmed to room temperature and was stirred for 72 hr. It was then quenched on 925 g of ice containing 50 ml of conc. hydrochloric acid. The mixture was stirred at 80-90 C. for 1 hr, cooled to room temperature, and extracted with methylene chloride. The organic layer was dried over magnesium sulfate, filtered, and solvent was removed under reduced pressure, leaving a yellow oil, which solidified overnight. GC and NMR showed this solid to be 97% p-n-dodecylacetophenone.

The acetophenone (187 g; 0.6287 mole) was then slurried in 275 ml of cyclohexane and charged slowly with phosphorus pentachloride (144 g; 0.69 mole), portionwise, keeping the temperature stabilized at 30 C. During the addition, there was copious evolution of HCl. After stirring for 1 hr at room temperature, the reaction mixture was

heated to 70 C. for 1 hr. At this point, GC indicated 95% product formation. The reaction mixture was cooled to room temperature, and solvent was removed under reduced pressure, leaving 208 g of a red oil (chloro products).

The chloro product mixture (208 g; 0.6287 mole) was dissolved in 175 ml of dry THF, cooled in an ice bath and charged during 2 hr with a slurry of potassium t-butoxide (157 g; 1.4 mole) in 500 ml of THF. The temperature during the addition was kept below 20 C. After the addition, the reaction mixture was refluxed for 5 hr. At this point, GC showed 76% product and 12% starting material. An additional 20 g of potassium t-butoxide was added, and the reaction mixture was refluxed an additional 4 hr. At this point, GC showed 87% product and 3% starting material. The reaction mixture solvent was evaporated under reduced pressure, leaving a dark brown gum. The gum was charged with 600 ml of hexane and 800 ml of water, giving an unsatisfactory split. Addition of magnesium sulfate, however, gave a clean split. The organic layer was dried over magnesium sulfate, filtered, and the solvent removed under reduced pressure, leaving 145 g of red oil, which was shown by GC to be 80% product and 13% impurity. HPLC purification led to the isolation of 84 g of an orange oil, identified by NMR and GC as p-n-dodecylphenylacetylene (est. purity 91%), which was used without further purification.

NMR (CDCl₃): 7.2 ppm, q, 4H (phenyl ring); 2.9 ppm, s, 1H (acetylenic); 2.5 ppm, t, 2H (benzyl); 1.2 ppm, broad s, 20H (methylene); 0.8 ppm, t, 3H (terminal methyl).

p-n-Hexylphenylacetylene (109a)

Phosphorus pentachloride (82.3 g; 0.39 mole) and p-n-hexylacetophenone (73.5 g; 0.36 mole) were stirred together in an ice water bath. An exotherm to 20 C. was noted. After the exotherm, the mixture was allowed to warm to room temperature and was stirred for 3 hr. GC indicated 83% product and 3% starting ketone. Solvent was evaporated under reduced pressure. The residue indicated 93% product by GC, wt. 98 g.

The above oil (98 g) was stirred and heated with KOH (85%; 149 g; 1.5 mole) and ethanol (350 ml). The mixture was refluxed overnight; GC showed 64% product. The reaction mixture was cooled, drowned in water, charged with ether, and the layers were split; the ether layer was washed with water and charged with acetic acid until neutral. Evaporation of solvent left 67 g of an oil. Distillation of this oil gave a major fraction having bp 86-88 C. @ 0.05 mm. This fraction weighed 25.3 g and was 93.6% pure by GC.

p-Bromophenylacetylene (63)

The procedure of Jacobs (43) was used with minor modifications. A mixture of p-bromoacetophenone (400 g; 2.01 mole) and phosphorus pentachloride (450.5 g; 2.163 mole) was heated to 70 C. and stirred, during which time there was vigorous evolution of HCl. The mixture was cooled to room temperature after 2.5 hr and the phosphorus oxychloride removed under reduced pressure. Distillation

of the residue afforded a 264 g fraction having bp 90-100 C. @ 3 mm. GC showed this fraction to be free of starting material and composed of the chloro product isomers. The chloro product mixture was charged with a solution of KOH (496.6 g) in ethanol (1360 g) and refluxed for 4 hr, cooled to room temperature, and quenched in 4 liters of ice water. The resulting oil was extracted with ether. The ether was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. Distillation of the residue without a condenser afforded 100 g of 94% pure p-bromophenylacetylene, mp 56-61 C.

3/4-(1,2-Dibromo)ethylbenzyl chloride (46)

Bromine (15.4 ml; 0.30 mole) was diluted with 50 ml of methylene chloride and added dropwise over a period of 45 min to a stirred solution of chloromethylstyrene (Dow Chemical Co., a 60/40 mixture of meta- and para- chloromethylstyrenes) (45.8 g; 0.30 mole) in 150 ml of methylene chloride. An ice bath was used initially to control the exotherm; as the yellow color became more persistent, the reaction was allowed to proceed at room temperature. After the addition of bromine was complete, the reaction was refluxed for 1 hr. Evaporation of solvent afforded 92.5 g of an off-white oil which formed a beige colored semi-solid upon prolonged standing. The oil was found to be >95% pure (GC) and was used without further purification.

NMR (CDCl₃): 7.5-7.2 ppm, d, 4H (aromatic); 5.2-4.9 ppm, q, 1H (CHBr);

4.5 ppm, s, 2H (CH₂Cl); 4.1-3.8 ppm, t, 2H (CH₂Br).

IR (neat): 1435, 1280, 705.

3/4-Ethynylbenzyl chloride (47)

A solution of potassium t-butoxide (18.0 g; 0.16 mole) in 75 ml of THF was added dropwise over a period of 45 min to a stirring solution of 3/4-(1,2-dibromo)ethylbenzyl chloride (23.4 g; 0.075 mole) in 50 ml of THF, maintained in a dry ice/acetone bath at -10 C. After the addition was complete, the suspension was stirred for 1 hr at -10 C., then for 18 hr at room temperature. Evaporation of solvent left a residue which was extracted with refluxing cyclohexane (3x75 ml). The extracts were combined and treated with activated charcoal. Evaporation of solvent left 10.2 g (90%) of a light yellow oil. GC indicated a purity of 95%, and the oil was used without further purification.

NMR (CDCl₃): 7.5-7.1 ppm, m, 4H (aromatic); 4.4 ppm, s, 2H (CH₂Cl); 3.1 ppm, s, 1H (acetylenic).

IR (neat): 3280, 1260, 800, and 710.

3/4-(Allyloxymethyl)phenylacetylene (52)

To a solution of 3/4-ethynylbenzyl chloride (22.6 g; 0.15 mole) and allyl alcohol (11.0 ml; 0.16 mole) was added 50% NaOH (80 ml; 1.5 moles NaOH), with cooling to control the exotherm. Approximately 20 ml of THF were added to make a stirrable suspension, followed by benzyltriethylammonium chloride (1.8 g; 0.0075 mole) (27). The suspension was stirred for 24 hr at 40 C. and then poured into 200

ml of ice water. The oily layer was separated, and the aqueous phase was extracted with methylene chloride (4x50 ml). The combined organic layers were washed with 50 ml of 5% aqueous acetic acid and then twice with 50 ml of water. The organic layer was dried with magnesium sulfate, and the methylene chloride was removed on a rotary evaporator, yielding 22.5 g of a dark oil which was extracted with hot methylcyclohexane (4x100 ml). Evaporation of solvent left a yellow oil which was distilled (bp 85-90 C., 0.8 mm) to yield 16.0 g (62%) of a pale yellow oil which was used without further purification.

NMR (CDCl₃): 7.6-7.1 ppm, m, 4H (aromatic); 6.2-4.9 ppm, m, 3H (vinylic); 4.4 ppm, s, 2H (allylic); 4.1-3.8 ppm, d, 2H (benzylic); 3.0 ppm, s, 1H (acetylenic).

IR (neat): 3275, 2850, 1080, and 795.

3/4-(Morpholinomethyl)phenylacetylene (48)

A stirred solution of 3/4-ethynylbenzyl chloride (15.1 g; 0.10 mole) and morpholine (17.5 ml; 0.20 mole) in 200 ml of toluene was refluxed for 18 hr under a nitrogen purge. The morpholinium hydrochloride was filtered and washed with hot toluene. The dark oil which resulted from the evaporation of the toluene was extracted with hot heptane. The combined extracts were treated with activated charcoal. Evaporation of solvent afforded 16.3 g (81%) of a light amber oil which was used without further purification.

NMR (CDCl₃): 7.5-7.0 ppm, m, 4H (aromatic); 3.7-3.5 ppm, m, 4H; 3.3 ppm, s, 2H; 3.0 ppm, s, 1H (acetylenic); 2.5-2.2 ppm, m, 4H.

IR (neat): 3275, 2920, 2850, 2800, 1115, 1010, and 865.

3/4[(1,4,7,10,13,16-Hexaoxaheptadecyl)methyl]phenylacetylene (41)

To a solution of 3/4-(chloromethyl)phenyl acetylene (7.5 g; 0.05 mole) and 3,6,9,12,15-pentaoxaheptadecanol (13.5 ml; 0.05 mole) was added 50% NaOH (27 ml; 0.5 mole); external cooling was required to control the exotherm. Addition of 40 ml of THF afforded a stirrable suspension to which benzyltriethylammonium chloride (0.57 g; 0.0025 mole) was added (27). The suspension was stirred at -10 C. for 18 hr and then filtered. The dark upper layer of the filtrate was extracted with THF (3x100 ml). Evaporation afforded a dark oil which was dissolved in 250 ml of methylene chloride, and then extracted with 5% aqueous acetic acid (50 ml) and then with water (2x50 ml). The organic layer was dried (magnesium sulfate), decolorized (Darco), and evaporated to a light yellow oil containing some water. The oil was treated for 90 min with boiling 2,2-dimethoxypropane to remove the water, and then solvent was evaporated to yield 17.1 g (93%) of a dry oil. This oil was used directly without further purification.

NMR (CDCl₃): 7.5-7.1 ppm, m, 4H (aromatic); 4.5 ppm, s, 2H (benzylic); 3.8-3.5 ppm, s, 2 OH (-CH₂CH₂O-); 3.3 ppm, s, 3H (-OCH₃); 3.2 ppm, s, 1H (acetylenic).

IR (neat): 3240, 2860, 1440, 1345, and 1100.

4-Ethylbenzenesulfonyl chloride (55)

A flask containing p-ethylbenzenesulfonic acid (93 g; 0.5 mole) was cooled in an ice bath while phosphorus pentachloride (104 g; 0.5 mole) was added portionwise. Much of the material dissolved during the highly exothermic reaction. Once the reaction subsided, the mixture was stirred for 30 min. Evaporation of the phosphorus oxychloride afforded 101 g (theoretical) of an amber oil. Distillation (105-110 C. @ 1.5 mm) yielded 63 g of a colorless oil. Anal. Calcd for C₈H₉ClO₂S: C, 46.94; H, 4.40; Cl, 17.35; S, 15.65.

Found: C, 46.39; H, 4.05; Cl, 16.82; S, 16.08.

NMR (CDCl₃): 8.1-7.2 ppm, q, 4H (aromatic); 3.1-2.5 ppm, q, 2H (-CH₂-); 1.5-1.1 ppm, t, 3H (-CH₃).

IR (neat): 1580, 1370, 1170, 835, and 645.

4-(1',1'-Dibromoethyl)benzenesulfonyl chloride (56)

N-Bromosuccinimide (89 g; 0.5 mole) and benzoyl peroxide (1.2 g; 0.005 mole) were added to a stirred solution of 4-ethylbenzenesulfonyl chloride (51.2 g; 0.25 mole) in 500 ml of carbon tetrachloride (previously refluxed to remove any traces of water). The suspension was maintained at 60 C. for 30 min and then refluxed for 2 hr (during which time the returning reflux became dark and then progressively lighter). The solution was filtered hot to remove succinimide. Evaporation of solvent afforded an amber semi-solid, which was extracted with hot petroleum ether (5x100 ml) and treated with activated charcoal. A white solid (42.6 g; 47%) was obtained after storage at -10 C. overnight, mp 53-57 C.

Anal. Calcd for C₈H₇Br₂ClO₂S: C, 26.50; H, 1.93; Cl, 9.80; S, 8.63.

Found: C, 26.69; H, 2.07; Cl, 8.11; S, 9.39.

NMR (CDCl₃): 8.0 ppm, s, 4H (aromatic); 3.0 ppm, s, 3H (-CH₃).

IR (Nujol): 1175 and 1055.

4-(1',1'-Dibromoethyl)-N,N-diphenylbenzenesulfonamide (57)

An intimate mixture of 4-(1',1'-dibromoethyl)benzenesulfonyl chloride (18.1 g; 0.05 mole), diphenylamine (8.5 g; 0.05 mole), and pyridine (6 ml; 0.075 mole) was heated over a steam bath. The mass became entirely liquid within a few minutes but solidified after an hour. Heating was continued for another 30 min, after which ice (100 g) was added to break up the solid, which was then washed with ice water (2x50 ml) followed by cold 2-propanol (50 ml). The solid was dissolved in hot methylcyclohexane, treated with activated charcoal, and filtered. A beige solid (23.1 g; 93%) precipitated upon cooling and was collected by filtration, mp 117-122 C. This solid was used without further purification in the preparation of 34.

NMR (CDCl₃): 8.0-7.5 ppm, q, 4H (aromatic); 7.2 ppm, s, 10H (aromatic); 2.9 ppm, s, 3H (CBr₂CH₃).

IR (Nujol): 1345, 1160, 710 and 700.

N,N-Diphenyl-4-ethynylbenzenesulfonamide (58)

A solution of potassium t-butoxide (9.5 g; 0.084 mole) in 75 ml of THF was added dropwise over a period of 45 min to a stirred solution of 4-(1',1'-dibromoethyl)-N,N-diphenylbenzenesulfonamide (19.7 g; 0.04 mole) in 150 ml of THF, a dry ice/acetone bath being employed to maintain the temperature at -10 C. The resulting suspension was stirred for 30 min at -10 C. and then stirred at room temperature for 18 hr. Evaporation of solvent left a dark-colored residue which was extracted with hot methylcyclohexane (5x50 ml). Evaporation of solvent afforded an off-white semi-solid (11.3 g; 85%) which was crystallized from methylcyclohexane, mp 124-127 C. Anal. Calcd for C₂₀H₁₅N₀S₂: C, 72.07; H, 4.50; N, 4.20; S, 9.61. Found: C, 72.21; H, 4.76; N, 4.69; S, 9.71. NMR (CDCl₃): 7.5 ppm, s, 4H (aromatic); 7.2 ppm, s, 10H (aromatic); 3.2 ppm, s, 1H (acetylenic). IR (Nujol): 3250, 1345, 1160, and 700.

Anthraquinone-2,6-disulfonyl chloride (78)

Following a literature procedure (34), anthraquinone-2,6-disulfonic acid, disodium salt (20.6 g; 0.05 mole) was converted to 54 with chlorosulfonic acid (85 ml; 1.29 mole). Recrystallization from toluene afforded the product (14.50 g; 72%) as yellow crystals, mp 248 C. (lit. (40), mp 250 C.). Anal. Calcd for C₁₄H₆C₁₂O₆S₂: C, 41.48; H, 1.48; Cl, 7.53; S, 15.80. Found: C, 41.27; H, 1.58; Cl, 16.82; S, 15.41. NMR (DMSO-d₆): 8.7 ppm, s, 2H (aromatic); 8.5-8.2 ppm, m, 4H (aromatic). IR (Nujol): 1685, 1585, 1375, 1300, 1190, 1155, and 960.

Anthraquinone-2,6-disulfonic acid, diphenyl ester (79)

In a modification of a literature procedure (50), anthraquinone-2,6-disulfonyl chloride (16.2 g; 0.04 mole) and phenol (8.3 g; 0.088 mole) were dissolved by heating to 85 C. in 400 ml of dioxane. The solution was rapidly cooled, and at 60 C. Sodium hydroxide (80 ml of 5N; 0.4 mole) was added as a stream to the rapidly stirring solution. The reddish gum that formed broke up into a discrete solid with continued stirring and cooling. Ice (200 g) was added, and the suspension was stirred for 30 min at ice temperature and then filtered under vacuum. The pink solid was washed with ice water (2x100 ml) and dried under vacuum. Recrystallization from hot ethoxyethanol afforded the product (16.5 g; 80%) as light yellow needles, mp 230 C. Anal. Calcd for C₂₆H₁₆O₈S₂: C, 60.00; H, 3.08; S, 12.31. Found: C, 59.92; H, 3.17; S, 11.71. Mass spectrum (EI): m/e 520 (M⁺) with losses of 93, 157, 64(SO₂) and 28(CO). NMR (DMSO-d₆): 7.5-7.2 ppm, m, 6H (AQ protons); 6.8-6.5 ppm, m, 10H (phenyl ester protons). IR (Nujol): 1680, 1590, 1395, 1290, 1195, 1140, 960, 920, 870, and 780.

2,6-Dihydroxyanthraquinone, bis(t-butyldimethylsilyl) ether (85)

A stirred solution of 2,6-dihydroxyanthraquinone (15.94 g; 0.0664 mole), imidazole (23.51 g; 0.3453 mole), and DMF (150 ml) was charged with t-butyldimethylsilylchloride (7) (25 g; 0.1659 mole) and stirred overnight. The reaction mixture was filtered to obtain a yellow solid, which was washed with methanol and dried, wt. 22 g. Recrystallization from methanol afforded 15 g of yellow needles, mp 137-138 C.

NMR (CDCl₃): 7.7 ppm, m, 6H (aromatic); 1.1 ppm, s, 18H (Si-t-Bu); 0.32 ppm, s, 12H (Si-Me).

IR: 1670 (AQ carbonyl).

2-Bromomethylantraquinone (71)

From 1700 ml of carbon tetrachloride, 200 ml was distilled off and discarded. To the remaining 1500 ml was added 2-methylantraquinone (95 g; 0.43 mole), N-bromosuccinimide (76 g; 0.46 mole), and 1.0 g of dibenzoylperoxide. The mixture was heated at reflux for 26 hr. TLC at this point showed some product but mainly starting material. TLC monitoring was continued, and an additional 1.0 g of dibenzoylperoxide was added at total reflux times of 26 hr, 44 hr, and 50 hr. After the final peroxide addition, refluxing was continued for an additional 18 hr. The reaction mixture was cooled to 5 C., filtered, and air-dried. The solid product mixture was slurried in 1 liter of water, and the slurry was heated to 85 C. and filtered hot. The solid thus obtained was slurried in another 1 liter of water; the slurry was heated to 55 C. and filtered; the product was air-dried. The weight of crude product was 58.2 g, mp 145-165 C. The crude product was recrystallized three times from acetic acid to give 20.3 g (15.7%) of 2-bromomethylantraquinone, mp 200-201 C., lit. (8) mp 200-201.

2-(N-Morpholinomethyl)anthraquinone (72)

2-Bromomethylantraquinone (20.0 g; 0.066 mole) was added to 350 ml of methylene chloride, followed by 35 ml of morpholine, which was added in one portion. The mixture was stirred overnight at room temperature. Solvent was removed on a rotary evaporator. The residue was triturated with a solution of 20 ml of 5N sodium hydroxide in 40 ml of water. The product, which at first oiled out, solidified and was filtered and dried under vacuum. The crude product was recrystallized from 340 ml of cyclohexane to give 8.3 g of 2-(N-morpholinomethyl)-anthraquinone, mp 103-104 C. Two additional crops gave an additional 2.6 g of material, mp 102.5-103.5 C. Thus the total yield of purified product was 10.9 g (54%).
Anal. Calcd for C₁₉H₁₇N₀3: C, 74.25; H, 5.58; N, 4.56.
 Found: C, 73.87; H, 5.66; N, 4.87.

Attempted preparation of 9,10-bis(phenylethyanyl)-2-dimethylamino-anthraquinone

A mixture of 12.6 g (0.05 mole) of 2-dimethylaminoanthraquinone (76), 11.2 g (0.109 mole) of phenylacetylene, 2.5 g (0.109 mole) of lithium amide, and 100 ml of dry dioxane was heated at reflux for 34

hr. The disappearance of starting material was monitored by TLC. At this point an additional 1.1 g of phenylacetylene and 0.25 g of lithium amide were added, and refluxing was continued for 3 hr. TLC indicated only a trace of starting material was present. The reaction mixture was poured into a mixture of 15 ml of acetic acid and 95 ml of water; an additional 100 ml of water was added. The two-phase mixture was extracted with 2 x 100 ml of methylene chloride. Solvent was evaporated from the organic layer, and the residue was triturated with 200 ml of ether. The resulting solid was filtered and air-dried to give 12.3 g of material. Reverse-phase TLC of this product showed that it was a mixture of at least five components. All attempts to isolate a pure component by recrystallization were unsuccessful.

A 1.0 g sample of the material was dissolved in 10 ml of DMF. Solid stannous chloride dihydrate (1.4 g) was added at room temperature, and the mixture was stirred for 4 hr. TLC of the reaction mixture at this point showed no fluorescent components present. Acetic acid (20 ml) was added, followed by 20 ml of 9N sulfuric acid. The reaction mixture was poured into 200 ml of water and filtered. The solid material thus obtained was not fluorescent and was therefore discarded.

3,3'-Benzophenonedisulfonyl chloride (100)

Following a literature procedure (40), benzophenone (92.0 g; 0.5 mole) was treated with chlorosulfonic acid (1175 g; 10.1 mole) to produce the desired compound. Recrystallization from hot toluene (first crop) or chloroform/hexane (second crop) afforded shiny, white crystals, mp 133-136 C. (lit. (46) mp 137-138 C.).
Anal. Calcd for C₁₃H₈C₁₂O₅S₂: C, 41.16; H, 2.11; Cl, 18.73; S, 16.89.

Found: C, 41.12; H, 2.27; Cl, 18.92; S, 17.84.

NMR (d-6 acetone): 8.5-7.8 ppm, m, 8H (aromatic).

IR (Nujol): 1660, 1590, 1420, 1370, 1265, 1170, 1080, and 980.

3,3'-Benzophenonedisulfonic acid, diphenyl ester

Following a modified literature procedure (50), 5N sodium hydroxide (20 ml; 0.10 mole) was added dropwise over a period of 40 min to a rapidly stirred, ice-cooled solution of 3,3'-benzophenone disulfonyl chloride (15.2 g; 0.04 mole) and phenol (7.5 g; 0.08 mole) in 125 ml of acetone. The resulting suspension was stirred for 24 hr at room temperature. After evaporation of solvent, the residue was poured onto cracked ice (200 g), forming a white oil which solidified upon stirring. The resulting white solid was filtered, washed with water (2x100 ml) and air-dried under vacuum, yielding 18.2 g of solid (90%). Recrystallization from n-butyl acetate afforded 16.0 g of a white crystalline solid, mp 128-132 C.
Anal. Calcd for C₂₅H₁₈O₇S₂: C, 60.73; H, 3.64; S, 12.96.

Found: C, 60.63; H, 3.79; S, 13.21.

NMR (d-6 acetone): 8.4-7.6 and 7.5-6.9 ppm (complex aromatic).

IR (Nujol): 1670, 1590, 1580, 1370, 1360, 1275, 1195, 1140, 990, 875, 860, 780, and 730.

3,3'-Benzophenone bis(N,N-diphenyl)sulfonamide (101)

Pyridine (150 ml) was added to an intimate mixture of N,N-diphenylamine (13.5 g; 0.08 mole) and 3,3'-benzophenone disulfonyl chloride (15.2 g; 0.04 mole). Heating on the steam bath with occasional swirling formed a homogeneous solution. After 60 min a solid precipitate formed, and heating was continued for an additional hour. Pyridine was removed on a rotary evaporator, and the resulting beige semi-solid was poured onto an ice-water mixture, precipitating a white solid which was collected by filtration. The solid was washed with ice water, air-dried under vacuum, and recrystallized from hot toluene after treatment with activated charcoal, mp 187-192 C.

Anal. Calcd for C₃₇H₂₈N₂O₅S₂: C, 68.94; H, 4.35; N, 4.35; S, 9.94.

Found: C, 70.24; H, 4.60; N, 4.10; S, 10.44.

NMR (DMSO-d₆): 8.5-8.0 ppm, s, 8H (benzophenone), 7.8-7.3 ppm, s, 10H (sulfonamide).

IR (Nujol): 1680, 1600, 1490, 1460, 1340, 1270, 1190, 1175, 1160, 1080, 990, 760, 750, and 740.

4,4'-Bis[(3,6,9,-trioxadecyl)oxy]benzophenone (105)

Following a modification of a literature procedure (42), a mixture of 4,4'dihydroxybenzophenone (4.3 g; 0.02 mole) and methoxytriglycol (Union Carbide, triethyleneglycol, monomethyl ether) (7.9 g; 0.048 mole) was heated with stirring to 90 C., at which time a thick, amber solution resulted. As the solution was cooling, N,N'-dicyclohexylcarbodiimide (9.1 g; 0.044 mole) was added portionwise, resulting in a homogeneous mixture. Under a nitrogen purge, the mixture was heated to 120 C. (bath temperature), forming a thick red solution. After 2 hr turbidity was noted; after 24 hr a precipitate had formed. Heating was continued for another 24 hr, and methylene chloride (100 ml) was added to the cooled suspension. Filtration, followed by washing with methylene chloride (4x50 ml), afforded 8.8 g (98%) of dicyclohexylurea (identified by IR). The filtrate was evaporated under reduced pressure to a dark oil, the TLC (50:EtOAc:50 methylene chloride:EtOAc of which showed almost total loss of starting material along with the formation of a major, much more polar component (the bis ether) and a minor, slightly more polar component (probably the mono-ether). The oil was taken up in 100 ml of hot toluene, treated with activated charcoal, and then evaporated under reduced pressure to a light oil. Elution of this oil through the HPLC (50:50 methylene chloride:EtOAc) and combination of the best fractions afforded 4.5 g (45%) of product.

NMR (CDCl₃): 7.8-6.7 ppm, q, 8H (p-substituted aromatic); 4.3-3.8 ppm, m, 8H (ArOCH₂CH₂); 3.8-3.4 ppm, d, 16 H (OCH₂CH₂); 3.3 ppm, s, 6H (CCH₃).

Mass spectrum: m/e (CI)=507.

IR (neat): 2870, 1640, 1600, 1300, 1250, 1165, 1100, 925, 850, and 770.

9,10-Bis(p-n-octylphenylethynyl)anthracene (23,BOBPEA)

A solution of 90.5% p-n-octylphenylacetylene (22.22 g; 0.0933 mole), lithium amide (2.4635 g; 0.1073 mole), and dry dioxane (160 ml) was stirred at 80 C. for 2.5 hr, cooled to room temperature, and charged with anthraquinone (9.2077 g; 0.0442 mole) and an additional 50 ml of dioxane. The reaction mixture was stirred at reflux for 40 hr, cooled to room temperature and charged with a solution of stannous chloride dihydrate (33.5 g) in 70 ml of DMF. The mixture was reheated to 100 C. and stirred for 5 hr, then cooled to room temperature and stirred overnight. The reaction mixture was then cooled to 10 C. and charged with 100 ml of glacial HOAc followed by 100 ml of dilute sulfuric acid, causing the formation of a dark brown, gummy tar. The supernatant liquid was decanted, and the tar was taken up in 200 ml of water and stirred for a half hour. It was decanted again, and the residue was dissolved in 400 ml of toluene and treated with Darco and magnesium sulfate. The mixture was brought to reflux, and water was removed via a Dean-Stark trap. It was filtered through Hyflo, and the solvent was removed under reduced pressure, leaving a dark brown semi-solid. Recrystallization from hexane afforded a yellow crystalline solid, 3.2 g, mp 131-133 C., TLC (4:1 hexane:methylene chloride, silica) showed one fluorescent green spot.

Anal. Calcd for C₄₆H₄₈: C, 91.64; H, 8.36.
Found: C, 92.15; H, 8.49.

Mass spectrum, M⁺ = 602, followed by loss of 99 (C₇H₁₅) twice.

NMR (CDCl₃): 8.1 ppm, d of q, 8H (anthracene ring H); 7.35 ppm, q, 8H (phenyl H); 2.6 ppm, t, 4H (benzyl H); 1.23 ppm, broad s, 24H (methylene); 0.85 ppm, m, (CH₃).

9,10-Bis(p-n-dodecylphenylethynyl)anthracene (24,BDDPPEA)

A solution of p-n-dodecylphenylacetylene (19.14 g; 0.0708 mole), lithium amide (1.8712 g; 0.0815 mole), and dry dioxane (135 ml) was stirred at reflux for 2.5 hr, cooled to room temperature, and charged with anthraquinone (6.9754 g; 0.0335 mole). The mixture was stirred at reflux overnight, cooled to room temperature, and charged with a solution of stannous chloride dihydrate (25.4 g) in 55 ml of DMF. The reaction was heated at 100 C. for 5 hr, cooled to room temperature, and charged with 150 ml of HOAc and 150 ml of dilute sulfuric acid, and then extracted with 400 ml of warm cyclohexane. The organic layer was dried over magnesium sulfate and charged with Darco and Hyflo and stirred 1 hr. It was filtered and evaporated under reduced pressure, leaving a brown solid. The solid was slurried in cold i-propanol, filtered, and washed with cold i-propanol to obtain 8.5 g of a bright yellow solid. TLC showed one major green fluorescent spot and a trace of AQ. Mass spectral analysis also revealed presence of AQ. Recrystallization from methylcyclohexane did not remove the AQ; however, HPLC purification using toluene as the eluent afforded 2.2 g of pure 9,10-bis(p-n-dodecylphenylethynyl)anthracene, mp 111-113 C. TLC showed a single component.

Anal. Calcd for C₅₄H₆₆: C, 90.70; H, 9.30.

Found: C, 90.41; H, 9.01.

Mass spectral analysis: M⁺ = 714 and two losses of 155, (C₁₁H₂₃).

NMR (CDCl₃): 8.2 ppm, d of q, 8H (anthracene ring); 7.55 ppm, q, 8H (phenyl rings); 2.73 ppm, t, 4H (benzyl); 1.3 ppm, broad s, 40H (methylene); 0.95 ppm, m, 6H (terminal methyl).

2,6-Dihydroxy-9,10-bis(phenylethynyl)anthracene,
bis(t-butyldimethylsilyl) ether (86)

A stirred suspension of phenylacetylene (6.2101 g; 0.0608 mole), lithium amide (1.5865 g; 0.0691 mole), and dry dioxane (130 ml) was refluxed for 2 hr, cooled to room temperature, and 13.5 g of the bis silyl ether 85 was added and the mixture refluxed for 5 hr. It was cooled to room temperature, charged with a solution of stannous chloride dihydrate (13 g) in 60 ml of DMF, and stirred overnight at room temperature. After cooling to 10 C., 70 ml of HOAc and 70 ml of dilute sulfuric acid were added successively, causing precipitation of a bright yellow solid. Washing with water and ethanol and subsequent drying afforded 13.8 g of yellow solid, which was shown by NMR, TLC, and MS to be a mixture of the mono- and di-silyl ethers. It was used in the following preparation without further purification.

2,6-Dihydroxy-9,10-bis(phenylethynyl)anthracene (87)

A stirred solution of the above silyl ether mixture (7.0 g; ca. 0.011 mole) in THF (250 ml) was cooled to 0 C. and charged dropwise over 0.5 hr with 66 ml of a 1M solution of tetra-butylammonium fluoride in THF (41). After the addition the reaction mixture was warmed to room temperature and stirred overnight. The mixture was charged with enough HOAc to produce an orange solution, which was evaporated under reduced pressure leaving a red oil. To this residue was added 250 ml of EtOAc causing precipitation of an orange solid (which was water-soluble). The EtOAc slurry was washed with water (3x500 ml). The organic layer was dried over magnesium sulfate, filtered, and the filtrate solvent removed under reduced pressure leaving 6 g of a brown solid. This solid was slurried in refluxing methylcyclohexane for 0.5 hr and filtered cold, affording 3.85 g of an orange solid. Recrystallization from 200 ml of i-propanol provided 2.9 g of an orange brown solid which was identified by TLC and MS as the desired product, mp >360 C. dec.

Anal. Calcd for C₃₀H₁₈O₂: C, 87.78; H, 4.42.

Found: C, 87.16; H, 4.82.

MS: M⁺ = 410.

IR: 3400-3100 (OH).

9,10-Bis(4'-bromophenylethynyl)anthracene-2,6-diphenylsulfonate (87)

A suspension of p-bromophenylacetylene (3.6208 g; 0.02 mole), lithium amide (0.4822 g; 0.021 mole), and dry dioxane (40 ml) was stirred at reflux for 2.5 hr, cooled to 15 C., and to this mixture was added anthraquinone-2,6-disulfonic acid, bis phenyl ester (55), (5.2 g; 0.01 mole) in 20 ml of dry dioxane. This mixture was stirred at reflux for 2 hr, cooled to room temperature, and stannous chloride dihydrate (7.5 g.) was added along with 5 ml of HOAc. This

mixture was refluxed for 20 hr, cooled to room temperature, slurried in 50 ml of dioxane, and filtered to obtain a red solid. This solid was stirred in hot toluene for 0.5 hr and filtered to remove insolubles. Upon cooling, the filtrate deposited 0.75 g of a red crystalline solid. The insolubles were re-extracted with hot toluene, and cooling the filtrate gave an additional 0.45 g of the solid. TLC (methylene chloride) revealed a single component present. The solid was identified as the desired compound, 58, 15% yield.

Anal. Calcd for C₄₂H₂₄Br₂S₂O₆: C, 59.45; H, 2.85; Br, 18.83; S, 7.56.

Found: C, 59.64; H, 3.18; Br, 16.72; S, 7.40.

Mass spectrum: M⁺ = 846 and two losses at 157 (SO₃Ph), as well as losses at 79 (Br) from these ions.

Attempted hydrolysis of 82 to the bis sodium salt, (83)

A mixture of the sulfonate ester (82) (0.15 g; 0.177 mole) and DMF (27 ml) was heated at 100 C., and to this solution was added sodium carbonate (0.0188 g; 37.5 mmole) in 2 ml of water. The mixture was stirred overnight at 105 C. and cooled to room temperature. A small aliquot was dissolved in water and gave a green fluorescent solution. TLC on reverse-phase silica (80/20:methanol/water) showed two major fluorescent components at R_f = 0.65 and 0.42, indicative of water soluble fluorescent salts.

9,10-Bis(4'-N,N-diphenylsulfonamidophenylethyne)anthracene (59)

A suspension of p-ethynyl-N,N-diphenylbenzenesulfonamide (7.2957 g; 0.0219 mole), lithium amide (0.5281 g; 0.023 mole), anthraquinone (2.1863 g; 0.0105 mole), and dry dioxane (50 ml) was stirred at reflux for 7 hr, cooled to room temperature, and stirred for two days. The mixture was charged with a solution of stannous chloride dihydrate (8 g) in 25 ml of DMF and 9 ml of HOAc. It was stirred at 90 C. for 3 hr, cooled to 10 C., and 45 ml of HOAc and 45 ml of dilute sulfuric acid were added, causing precipitation of 4 g of an orange solid, which was washed successively with water, ethanol, and hexane and dried. Recrystallization from chlorobenzene afforded 2 g of an orange solid; TLC indicated ca. 95% purity. IR and NMR confirmed the structure as the desired product, 59.
NMR (CDCl₃): 8.2 ppm, d of q, 8H (anthracene ring); 7.8 ppm, q, 8H (phenyl rings); 7.32 ppm, s, 20H (N-phenyl rings).
IR (Nujol): 2200, 1350, and 1160 (SO₂).

Attempted hydrolysis of 59 to the bis sodium sulfonate, (60)

A suspension of sodium metal (as a 40% mineral oil dispersion, 2.6813 g; 0.0467 mole) and i-amyl alcohol (11.25 ml) was stirred at reflux for 6 hr until a solution resulted, charged with 60 (1.0 g; 1.19 mole), and stirred at reflux overnight (28). The reaction mixture was cooled to room temperature, charged with 20 ml of HOAc and 20 ml of water, and stirred, becoming a turbid yellow. Solvent was removed under reduced pressure, leaving a yellow solid. This solid was stirred in hot DMF for 1 hr and filtered hot to remove insolubles. Removal of solvent under reduced pressure left a yellow-orange solid. TLC of this solid using reverse-phase C18

silica (80/20: ethanol/water) showed one major and several minor components, all having R_f values indicative of fluorescent salts. Attempted purification by HPLC afforded an orange solid which gave an unsatisfactory elemental analysis (sodium too high).

9,10-Bis(p-bromophenylethyanyl)anthracene (64), BRBPEA

p-Bromophenylacetylene was prepared from p-bromoacetophenone by a modification of the procedure described in Organic Reactions (53), using potassium t-butoxide in DMSO for the dehydrochlorination step. The NMR spectrum of the product was consistent with the structure. Anthraquinone (3.74 g; 0.018 mole) was added to 50 ml of dry dioxane along with 7.2 g (0.04 mole) of p-bromophenylacetylene and 0.92 g (0.04 mole) of lithium amide. The heterogeneous mixture was then heated with stirring under an argon atmosphere for 24 hr. The cooled reaction mixture was then poured carefully into 700 ml of distilled water, acidified with acetic acid, and a brown solid filtered. The yield of crude product was 10.1 g. TLC of the product indicated only a trace of anthraquinone remaining unreacted. A portion (9.6 g) of this solid was dissolved in 20 ml of DMF, and to the solution was added 11.4 g (0.0504 mole) of stannous chloride dihydrate. This mixture was stirred for 2 hr at room temperature followed by 1 hr at 55 C. After standing at ambient temperature, a bright orange solid was filtered and washed two times with methanol, yielding 7.2 g of crude product. The crude product was dissolved in 400 ml of boiling chlorobenzene, Magnesol was added, and the mixture was filtered. The flask was purged with argon during this recrystallization. The filtrate was concentrated to 225 ml, and bright orange needles precipitated on cooling. The solid was filtered, washed once with chlorobenzene, three times with methanol and air-dried. The yield was 6.0 g (62%), mp 295-297.

Anal. Calcd for C₃₀H₁₆Br₂: C, 67.19; H, 3.01; Br, 29.80.

Found: C, 66.95; H, 3.15; Br, 27.26.

Mass spectrum: M⁺ = 534; M-HBr = 454; M-2HBr = 374.

Fluorescence max. at 485 nm in dibutyl phthalate (conc. .002M)

9,18-Bis(p-carboxyphenylethyanyl)anthracene, bis lithium salt (18)

A suspension of BRBPEA (64) (7.0 g; 0.0131 mole), chlorobenzene (630 ml), and 34.9 ml of 1.5M n-BuLi in hexane was stirred at room temperature, heated to 75 C. during 45 min, and kept at 75 C. for 1.5 hr. The suspension was cooled to room temperature and treated during 1.5 hr with a vigorous stream of CO₂ gas. This caused precipitation of an orange solid (9.2 g), which was filtered, washed with methylene chloride, and air-dried. TLC analysis of this solid using reverse-phase C18 silica (80/20:ethanol/water) showed one major green fluorescent component and two minor blue fluorescent components. Recrystallization of 4 g of this solid from 200 ml of water afforded a very small amount of an orange solid. TLC of this solid showed a trace of one of the blue components. This compound was tested as such for chemiluminescent activity in water with and without surfactant.

9,10-Bis[3/4-(morpholinomethyl)phenylethyanyl]anthracene (50)

A suspension of lithium amide (1.1 g; 0.048 mole) and 3/4-(morpholinylmethyl)phenylacetylene (48) (8.8 g; 0.044 mole) in 100 ml of dioxane was refluxed under a nitrogen purge for 3 hr. The suspension was cooled to 15 C., and anthraquinone (4.1 g; 0.02 mole) was added along with an additional 25 ml of dioxane. The suspension was refluxed for 18 hr and cooled to room temperature. A slight exotherm occurred during the addition of 50% aqueous HOAc (10 ml), followed by a solution of stannous chloride dihydrate (3.5 g) in DMF (25 ml). The solution was stirred at room temperature for 24 hr, and solvent was removed on a rotary evaporator. The yellow solid which resulted from the addition of 20 ml of 5N sulfuric acid, followed by 80 ml of ethanol, was filtered and washed with ethanol (2x25 ml). This solid was dissolved in hot water; addition of 5N NaOH caused the precipitation of a gummy solid which was collected and dissolved in hot toluene. Evaporation of toluene afforded a red semi-solid which was extracted with hot methylcyclohexane. After treatment with activated charcoal, an orange solid precipitated from solution and was collected by filtration, mp 150-168.

Anal. Calcd for C₄₀H₃₆N₂O₂: C, 83.33; H, 6.25; N, 4.86.

Found: C, 83.97; H, 6.15; N, 4.38.

NMR (CDCl₃): 8.8-7.1 ppm, two sets of multiplets, 16H (aromatic); 3.8-3.5 ppm, m, 8H (ring methylenes); 3.4 ppm, s, 4H (benzylic); 2.5-2.2 ppm, m, 8H (ring methylenes).

IR (Nujol): 1110, 1005, 885, and 775.

9,10-Bis[3/4-(morpholinomethyl)phenylethynyl]anthracene, dimethyl sulfate quaternary (51)

To an ice cooled solution of 50 (2.9 g; 0.005 mole) in 50 ml of ethylene dichloride was added dropwise over a period of 20 min, dimethyl sulfate (1.0 ml; 0.01 mole) diluted with 10 ml of ethylene dichloride. The clear solution was stirred at ice temperature for 30 min, then at room temperature for 1 hr, and then refluxed for 18 hr. The yellow precipitate which formed was filtered, washed with ethylene dichloride (2x50 ml), hexane (2x50 ml), and then air-dried under vacuum, mp 254-260 C.

Anal. Calcd for C₄₄H₄₈N₂O₁₀S₂: C, 63.77; H, 5.80; N, 3.34; S, 7.73.

Found: C, 61.82; H, 6.00; N, 3.36; S, 7.47.

IR (Nujol): 1215, 1120, 1060, 1000, 890, and 725.

9,10-Bis[3/4-(hydroxymethyl)phenylethynyl]anthracene (54)

To a stirred solution of 53 (5.2 g; 0.01 mole) in 75 ml of dioxane was added selenium(IV)dioxide (2.4 g; 0.022 mole) and glacial acetic acid (1.8 ml; 0.03 mole). After 3.5 hr TLC (50/50 methylene chloride:EtOAc) revealed almost complete loss of starting material. The solution was filtered hot to remove a black solid, which was washed with hot dioxane (2x50 ml). Evaporation of solvent afforded an orange semi-solid. Elution of this material through a Waters Prep 500 HPLC (2:1 CHCl₃/THF) afforded the pure compound as the most polar fraction of the mixture, mp 160-169.

Anal. Calcd for C₃₂H₂₂O₂: C, 87.67; H, 5.02.

Found: C, 85.07; H, 5.55.

Mass spectrum (E/I): 438 (M⁺).

NMR (DMSO-d₆): 8.6-7.0 ppm, complex m, 16H (aromatic); 4.5 ppm, broad s, 2H (OH, exchanged with D₂O) and 3.3 ppm, s, 4H (benzylic).
 IR (Nujol): 3250, 1600, 1260, 760, and 640.

9,10-Bis[3/4-(allyloxymethyl)phenylethynyl]anthracene (53)

A suspension of 52 (11.4 g; 0.066 mole) and lithium amide (1.6 g; 0.072 mole) was refluxed for 4 hr in 125 ml of dioxane under a nitrogen purge. The suspension was cooled to 15 C., and anthraquinone (6.2 g; 0.03 mole) was added, followed by an additional 50 ml of dioxane. The mixture was stirred at reflux for 18 hr and then cooled to room temperature. A slight exotherm ensued upon the addition of 50% aqueous HOAc (9 ml), followed by the addition of stannous chloride dihydrate (20 g; 0.09 mole) dissolved in 80 ml DMF. The solution was stirred at room temperature for 4 hr and then cooled in an ice bath. A yellow-brown solid (gummy at first, gradually becoming granular with continued stirring) formed upon the addition of glacial HOAc (50 ml) and 5N sulfuric acid (50 ml). The solid was collected by filtration, washed with water, and then air-dried under vacuum. The solid was dissolved in hot methyliccyclohexane and treated with Magnesol and Darco. A bright yellow solid crystallized upon cooling, mp 55-62.
Anal. Calcd for C₃₈H₃₀O₂: C, 88.03; H, 5.79.

Found: C, 88.48; H, 5.89.

NMR (CDCl₃): 8.8-7.2 ppm, two multiplets, 16H (aromatic); 5.8-4.8 ppm, m, 3H (CH₂::CH₂); 4.6-4.3 ppm, m, 2H (benzylic) and 4.2-3.8 ppm, m, 2H (allylic).

IR (Nujol): 1595, 1340, 1080, 1010, 930, 800, and 760.

9,10-Bis[3/4-(sodiosulfatomethyl)phenylethynyl]anthracene (20)

A stirred solution of 54 (1.1 g; 0.0025 mole) and sulfur trioxide trimethylamine complex (0.7 g; 0.005 mole) was refluxed in acetonitrile for 24 hr. TLC (20% aqueous acetonitrile) showed almost complete loss of starting material concurrent to the formation of a more polar product. The reaction was cooled to ice temperature, and 5N NaOH (1 ml; 0.005 mole) was added dropwise, causing the immediate formation of an orange precipitate and a strong ammoniacal odor. The solid was collected by filtration and washed with acetonitrile (2x25 ml), mp >350 C., some decomposition.
 IR (Nujol): 1590, 1170 (center of broad peak), and 760.

9,10-Bis(phenylethynyl)anthracene-2,6-disulfonic acid, diphenyl ester (80)

A mixture of phenylacetylene (2.3 ml; 0.02 mole) and lithium amide (0.5 g; 0.021 mole) in 40 ml of dioxane was refluxed under a nitrogen purge for 4 hr and then cooled to 15 C. The flask was then charged with anthraquinone-2,6-disulfonic acid, diphenyl ester (5.2 g; 0.01 mole) and 20 ml of dioxane, and refluxed for 19 hr. The solution was cooled to room temperature, and stannous chloride dihydrate (4.5 g; 0.02 mole) dissolved in 25 ml of glacial HOAc was added. The solution was refluxed for 5 hr. Upon cooling to room temperature, an orange-red solid precipitate formed and was collected by filtration. The solid was recrystallized from hot DMF; yield 1.1

g, mp 244-247.

Mass spectrum (EI): m/e 690 (M^+) with losses of 157 twice (PhSO_3).
IR (Nujol): 1190, 1175, 1150, 865, 780, and 695.

Attempted hydrolysis of 9,10-bis(phenylethynyl)anthracene-2,6-disulfonic acid diphenyl ester (80)

To an ice-cooled solution of bis(phenylethynyl)anthracene-2,6-disulfonic acid, diphenyl ester (80), (0.69 g; 0.001 mole) in 50 ml of DMF (required heat to dissolve), was added 5N NaOH (4 ml; 0.02 mole). The solution was refluxed for 20 hr and cooled. The solvent was removed on a rotary evaporator, and 5N HCl was added dropwise to the resulting brown semi-solid until neutral to pH test paper. The material solidified upon standing, but reverse-phase TLC (20% aqueous acetonitrile) revealed a number of polar spots, including a green fluorescer, a blue fluorescer, and a quencher, but no starting material. The material could not be recrystallized from common polar solvents. It was therefore eluted through the preparative HPLC (reverse-phase; 20% aqueous acetonitrile). The material obtained was still not pure (TLC), but was soluble in water, giving a green fluorescent solution.

9,10-Bis[3/4-(1,4,7,10,13,16-hexaoxaheptadecylmethyl)phenylethynyl]-anthracene (66)

A mixture of 3/4-(1,4,7,10,13,16-hexaoxaheptadecylmethyl)-phenylacetylene (65) (18.3 g; 0.05 mole) and lithium amide (1.3 g; 0.055 mole) in 75 ml of dioxane was refluxed under a nitrogen atmosphere for 3 hr. The solution was cooled to 20 C. and anthraquinone (5.2 g; 0.025 mole) was added along with 25 ml of fresh dioxane; refluxing was continued for 4 hr. After cooling to room temperature, 15 ml of aqueous HOAc, followed by stannous chloride dihydrate (11.3 g; 0.05 mole) dissolved in 35 ml of DMF, was added. The solution was stirred 20 hr at room temperature and then cooled in an ice bath. A gummy material, displaying inverse solubility behavior (i.e., more soluble when cold), formed upon the addition of 50 ml of glacial HOAc, 50 ml of 5N sulfuric acid, and 200 ml of water. The aqueous layer was heated and extracted with hot toluene (5x70 ml) as the upper layer of the rapidly stirring two-phase system. The combined toluene fractions were treated hot with Magnesol, then Darco, and finally anhydrous magnesium sulfate. Removal of solvent left a dark oil, highly chemiluminescent in the organic system, moderately in the aqueous system. The oil was purified by HPLC (3:1 EtOAc:acetone), yielding an orange oil (single spot on TLC). Spectral evidence was consistent with the expected structure.

NMR (CDCl₃): 8.8-8.4 ppm and 7.8-7.2 ppm, two sets of multiplets, 16H (aromatic); 4.7-4.4 ppm, s, 4H (benzylic); 3.7-3.4 ppm, s, 20H (-CH₂CH₂O-); 3.2 ppm, s, 3H (-OCH₃).

IR (neat): 2860, 1595, 1435, 1345, 1240, 1100, 770, 735, and 695.

2,6-Bis[(2'-trimethylammonium)ethoxy]-9,10-bis(phenylethynyl)anthracene, methosulfate (69)

To 4.08 g of 2,6-bis(2'-dimethylaminoethoxy)anthraquinone (68) bis HCl salt dihydrate (Aldrich 21,806-5) dissolved in 75 ml of distilled water was added 3 ml of 5N NaOH. A yellow solid separated as very fine particles. The solid was filtered, washed with water, and dried in vacuo. A second crop was obtained by partial evaporation of the filtrate and addition of more 5N NaOH. Total weight of both crops was 3.32 g (quant. yield). NMR of the diamine was consistent with the expected structure.

The diamine prepared above (2.60 g; 6.80 mmole) was added to 50 ml of dioxane along with 3.0 ml (27.2 mmole) of phenylacetylene and 0.63 g (27.2 mmole) of lithium amide under an argon atmosphere. The reaction mixture was then heated with stirring at reflux for 40 hr. The cooled reaction mixture was added carefully to 300 ml of distilled water and extracted with chloroform/ether followed by chloroform alone. Evaporation of the solvent under reduced pressure left a dark brown oil. This oil was dissolved in 10 ml of DMF. To the solution was added a solution of 4.6 g (20.4 mmole) of stannous chloride dihydrate. The mixture was stirred for 2 hr and allowed to stand for 4 days at ambient temperature. Adding the reaction mixture to water gave a finely dispersed precipitate which was filtered (slowly) with suction. An attempt to isolate the product via liquid-liquid extraction was unsuccessful. The addition of 5% potassium carbonate solution to the washings gave a more easily filtered solid. Some amine hydrochloride may have caused the filtration problem. After washing with water and drying, the crude product was recrystallized from toluene, yielding 1.2 g of an orange solid. TLC indicated that some impurities were still present, so the solid was further purified by preparative HPLC on silica using 1:1 acetone-methanol as eluent. The middle cuts containing the product were chromatographed a second time using methanol as eluent. Analysis of the cuts by TLC and combining gave, after evaporation, 0.91 g of a bright orange solid which was dissolved in 20 ml of dichloromethane, and 0.31 ml of dimethyl sulfate was added. An orange solid precipitated within a few minutes. An additional 10 ml of solvent was added and the mixture cooled in a refrigerator overnight. After 3 days the solid was isolated by filtration, washed with dichloromethane, and air-dried, yielding 1.32 g of a yellow solid. After Soxhlet extraction and recrystallization from methanol, bright yellow platelets were obtained (mp >300).
Anal. Calcd for C₄₂H₄₈N₂S₂O₁₀: C, 62.66; H, 6.01; N, 3.48; S, 7.96.
Found: C, 62.93; H, 6.15; N, 3.67; S, 7.39.

9,10-Bis(phenylethynyl)-2-(N-morpholinomethyl)anthracene (73)

A mixture of phenylacetylene (3.1 g; 0.03 mole), lithium amide (0.7 g; 0.03 mole), and 75 ml of dry dioxane was heated at reflux for 4 hr. 2-(N-morpholinomethyl)anthraquinone (2.1 g; 0.0068 mole) was added; the color of the solution changed from yellow to dark red. The reaction mixture was heated at reflux for 28 hr. Solvent was removed on a rotary evaporator. To the residue was added a solution of 2 ml of acetic acid in 50 ml of water. The product was filtered, washed with water, then with hexane, and air-dried. Reverse-phase TLC indicated that the mixture contained a major component and a minor component. The yield of crude product was 5.6 g. A portion of this product (2.0 g) was dissolved in 25 ml of dioxane, and a solution of 3.1 g of stannous chloride dihydrate in 35 ml of 50% aqueous acetic acid was added dropwise during 5 min. The reaction mixture was stirred for 1.5 hr at room temperature. The tacky product was filtered and dissolved in 50 ml of methylene chloride. Solvent was stripped off on a rotary evaporator, and the now solid product was combined with a second crop of material isolated from the filtrate of the original reaction mixture. The total yield of material isolated was 0.3 g. This material was dissolved in 5 ml of methylene chloride and was eluted through a silica column. The major band came off with 9% methanol in methylene chloride. Solvent was evaporated to give 0.1 g of product. Mass spectral analysis showed that this product was a mixture of 9,10-bis-(phenylethynyl)-2-(N-morpholinomethyl)anthracene (49) and its hydrochloride (50).

5,6,11,12-Tetraphenyl-2,8,3',3'''-tetra(N,N-diphenylsulfamoyl)-naphthacene (104)

A suspension of phenylacetylene (2.2 ml; 0.02 mole) and lithium amide (0.5 g; 0.022 mole) was refluxed in 75 ml of dioxane under a nitrogen purge for 4 hr. The suspension was cooled to 15 C., and 3,3'-benzophenone-bis(N,N-diphenylsulfonamide) (12.9 g; 0.02 mole) and 25 ml of dioxane were added. After refluxing for 30 min, an aliquot was removed, and IR showed no carbonyl present. Reflux was continued for an additional 45 min, the reaction was cooled, and glacial HOAc (1.5 ml) was added dropwise. The lithium acetate precipitate was filtered, and dioxane was removed from the filtrate under reduced pressure. The resulting thick, beige oil solidified into a mass upon standing 24 hr at room temperature. The solid (14.8 g; theoretical) was deemed to be of sufficient purity to be used as such. A small sample was recrystallized from methylcyclohexane to a white powder, mp 56-60. The IR spectrum of the product was consistent with the expected structure.

Anal. Calcd for C₄₅H₃₄N₂O₅S₂: C, 72.39; H, 4.56; N, 3.75; S, 8.58.

Found: C, 73.02; H, 5.04; N, 4.77; S, 10.18.

IR (Nujol): 3450, 3060, 2850, 2225, 1590, 1480, 1420, 1360, 1260, 1160, 970, 910, 875, 805, and 760.

A solution of the above carbinol (7.5 g; 0.01 mole) in methylene chloride was cooled in an ice/acetone bath for one hour. A solution of thionyl chloride (1.1 ml; 0.015 mole) in 10 ml of

methylene chloride was added dropwise over a period of 30 min to the rapidly stirring solution. The resulting solution was stirred for 1 hr at ice temperature and then 1 hr at room temperature. A tan solid formed upon removal of solvent, the IR of which displayed only a slight trace of a hydroxyl peak. This material was used in the next step with no further purification.

IR (Nujol): 1580, 1340, 1150, 970, 760, and 700.

A solution of crude 1,1-bis[3,3'-(diphenylsulfamoyl)phenyl]-3-phenyl-2-propynyl-1-chloride (5 g; 0.0065 mole) and quinoline (0.5 ml; 0.0042 mole) in 20 ml of xylene was refluxed under a nitrogen purge for 24 hr, during which time an orange precipitate formed. The solution was cooled in an ice bath, and the solid was collected by filtration, washed with cold xylene (25 ml) and hexane (2x25 ml), and then air-dried under vacuum, mp 342-350, some decomposition. The IR spectrum was consistent with the expected structure, although the elemental analysis was not acceptable.

IR (Nujol): 1585, 1350, 1260, 1160, 1080, 970, and 700.

2,8,4'',4'''-Tetra(trioxadecyloxy)rubrene (108)

A suspension of lithium amide (0.2 g; 0.009 mole) and phenylacetylene (0.9 ml; 0.0083 mole) in 30 ml of dioxane was refluxed under a nitrogen atmosphere for 4 hr. The solution was cooled to 15 C., and 4,4'-bis[(3,6,9-trioxadecyl)oxy]benzophenone (3.75 g; 0.0075 mole) was added. The solution was refluxed for 24 hr and cooled to room temperature. Addition of glacial HOAc (0.6 ml) caused precipitation of lithium acetate, which was removed by filtration. Solvent was removed under reduced pressure, and the resulting amber oil displayed a strong hydroxyl band in the IR and almost no carbonyl. This material was used without further purification.

The entire oil was dissolved in 50 ml of methylene chloride and cooled in an ice/alcohol bath. Thionyl chloride (0.8 ml; 0.011 mole) diluted in 10 ml of methylene chloride was added dropwise over 30 min to the stirred solution, which was stirred for 1 hr at ice temperature and 1 hr further at room temperature. Solvent was removed under reduced pressure, and the resulting brown oil showed complete loss of the hydroxyl band in the IR spectrum. This material was used without further purification.

The above oil was dissolved in 35 ml of xylene, to which quinoline (0.4 ml; 0.0035 mole) was added. The solution was refluxed under a nitrogen atmosphere for 24 hr, at which time the solution displayed a strong red fluorescence upon exposure to a long-wave UV source. Solvent was removed under high vacuum to yield a red-brown oil, the TLC of which showed one strong, red fluorescer along with a number of minor impurities. Elution of the sample through the HPLC (2:1 methylene chloride/methyl ethyl ketone), followed by combination of the appropriate fractions and evaporation afforded a thick, red oil, highly fluorescent and chemiluminescent in both organic and aqueous media.

IR (neat): 2875, 1600, 1450, 1345, 1240, 1120, 950, 845, and 700.

5,11-Bis[3'/4'-(hexaoxaheptadecyl)methylphenyl]-6,12-diphenylnaphthalene (15)

A suspension of 3/4-(hexaoxaheptadecyl)methylphenylacetylene (22.0 g; 0.05 mole) and lithium amide (1.7 g; 0.072 mole) was stirred under a nitrogen atmosphere in 200 ml of refluxing dioxane for 4 hr. The suspension was cooled, benzophenone (10.9 g; 0.06 mole) was added, and refluxing was continued for 20 hr. The solution was cooled, and HOAc (5 ml) was added, causing the precipitation of lithium acetate, which was removed by filtration. Solvent was removed under reduced pressure, and the dark residue was extracted with hot toluene, treated with activated charcoal, and evaporated under reduced pressure to give an amber oil. The IR spectrum of this material showed only a trace of carbonyl remaining; it was used in the propynyl chloride preparation without further purification.

This material was taken up in 200 ml of methylene chloride, and the solution was cooled to -5 C. in an ice/acetone bath. A solution of thionyl chloride (6.6 ml; 0.09 mole) diluted with 15 ml of methylene chloride was added dropwise over 20 min to the stirred solution. The temperature was held at 0 C. for 1 hr and held at room temperature for 2 hr. Solvent was removed under reduced pressure, leaving a residue which displayed virtually no hydroxyl band in the IR spectrum. This material was used without further purification in the preparation of the rubrene derivative.

The above oil was dissolved in 50 ml of chlorobenzene and protected from light. Quinoline (3 ml; 0.025 mole) was added, and the solution was refluxed under a rapid nitrogen purge for 28 hr. Solvent was removed under high vacuum, leaving a brown oil (30 g) which had good chemiluminescence in the aqueous/surfactant system. The TLC of this material showed a large number of spots, including three closely-spaced orange fluorescers. Using a 4:1 methyl ethyl ketone/THF solvent system, 8 g of this material were eluted through the HPLC. Evaporation of solvent produced an orange-red oil (5 g). The later fractions were of higher purity (both via TLC and also from quantitative chemiluminescence measurements in the aqueous system), but some contamination with a blue fluorescer and a fluorescence quencher remained.

IR (neat): 2860, 1600, 1440, 1345, 1290, 1240, 1100, 780, and 700.

5,12-Bis[3/4-(morpholinomethyl)phenyl]-14,11-diphenylnaphthacene (14)

A suspension of lithium amide (1.4 g; 0.06 mole) and 3/4-(morpholinomethyl)phenylacetylene (12.1 g; 0.06 mole) was refluxed in 75 ml of dioxane, under a nitrogen atmosphere, for 3 hr. The suspension was cooled to 15 C., and benzophenone (10.9 g; 0.06 mole) was added, along with 50 ml of dioxane. The solution was refluxed for 3 hr and cooled to room temperature. Addition of acetic acid caused the precipitation of lithium acetate, which was removed by filtration. Solvent was removed on a rotary evaporator, leaving a honey-colored oil, the TLC and IR of which indicated a mixture of benzophenone and carbinol. Separation was achieved using HPLC with a 4:1 methylene chloride/EtOAc system as eluent, yielding a light yellow oil (14.7 g; 65%). Some of the material crystallized out, in

two separate fractions (possibly the two isomers), from hot methylcyclohexane.

A solution of 3/4-(morpholinomethyl)phenyl-1,1-diphenyl-propyn-1-ol (7.6 g; 0.02 mole) was dissolved in 80 ml of methylene chloride and chilled to -5 C. in an ice/acetone bath. Over a period of 50 min, thionyl chloride (1.8 ml; 0.024 mole) diluted in 20 ml of methylene chloride was added to the stirred solution. The solution was kept at ice temperature for 2 hr and allowed to stir and come to room temperature for 2 hr, at which time the IR spectrum displayed complete loss of -OH. Removal of solvent under reduced pressure caused the formation of a tan solid (gummy at first, becoming powdery). The yield (8.5 g) and the solubility (insoluble in non-polar solvents, soluble in water and alcohols) indicated that the compound was isolated as the bis-hydrochloride salt. This material was used in its crude form in the rubrene synthesis.

The above propynyl chloride (6.0 g; 0.014 mole) was dissolved in 30 ml of DMF, and silica gel (6.0 g) was sifted in to form a suspension. Under a rapid nitrogen purge, this suspension was refluxed for 48 hr, during which time a red fluorescence under long wave UV light could be detected. The suspension was filtered hot, and the silica gel was washed with hot DMF (2x25 ml). A brown oil resulted from the evaporation of solvent under reduced pressure, a sample of which displayed a strong chemiluminescence in both the organic and aqueous systems. The oil was dissolved in water (completely soluble); dropwise addition of 5N NaOH caused the precipitation of a red-pink solid, which was collected by filtration, washed with water (2x50 ml), and air-dried under vacuum. The TLC showed a large number of fluorescent and quencher spots. Using a 4:1 acetonitrile/methyl ethyl ketone eluent, HPLC afforded a fraction which contained a single orange fluorescer and a slight contamination of a blue fluorescent impurity. Mass spectrometry revealed a strong molecular ion at m/e 730, consistent with the expected structure. To this amine (0.26 g; 0.37 mmole) in 25 ml of methylene chloride was added 0.07 ml (0.74 mmole) of dimethyl sulfate and the solution refluxed overnight in order to obtain a water-soluble rubrene.

4',4'''-Di-n-hexylrubrene (27a)

Under an argon atmosphere, p-n-hexylphenylacetylene (24 g; 0.12 mole), lithium amide (5.8 g; 0.24 mole), and dioxane (200 ml) were stirred for 2 hr at room temperature. The suspension was stirred, charged with benzophenone (21.8 g; 0.12 mole), and heated at reflux for 3 hr. IR indicated the absence of any carbonyl. The reaction mixture was cooled and drowned in water, charged with ether, and the layers were separated. The ether layer was dried over magnesium sulfate, filtered, and evaporated under reduced pressure, leaving 42.7 g of an amber oil.

This oil was dissolved in petroleum ether (50 ml) and cooled to -10 C. by an ice/methanol bath. Thionyl chloride (26.2 g; 0.22 mole) was added during 45 min at -5 C. to 0 C. The ice bath was removed, the reaction mixture, warmed to room temperature, and the solvent removed under reduced pressure. Pet ether (50 ml) was added

to the residue and evaporated under reduced pressure to yield an oil which had no hydroxyl band in the IR.

The above oil was stirred under argon with quinoline (2 ml) and chlorobenzene (50 ml). This mixture was refluxed overnight and cooled to room temperature. TLC showed one major red spot and several minor spots. The solvent was removed under reduced pressure and gave 42.7 g of a thick red oil. The oil was dissolved in refluxing i-propanol, treated with Darco and Hyflo, filtered, and cooled slowly. Filtration of the cooled filtrate afforded 14 g of a semi-solid, which was shown by TLC to be unchanged. Purification of 10 g of this semi-solid using HPLC and cyclohexane as the eluent provided three fractions having similar TLC. These were combined, and solvent was removed, affording 1.0 g of a red solid. Recrystallization of this solid from methyl cellosolve afforded 0.3 g of red crystals, one component by TLC. These crystals exhibited strong chemiluminescence in the organic system.

4',4'''-Di-n-octylrubrene (27b)

Under an argon atmosphere, a mixture of p-n-octylphenylacetylene (23.8 g; 0.1 mole), lithium amide (4.8 g; 0.2 mole), and dioxane (200 ml) was stirred at room temperature for 2 hr. A solution of benzophenone (18.2 g; 0.1 mole) in 100 ml of dioxane was added. No exotherm was noted, and the mixture was heated at reflux for 22 hr, at which time IR indicated almost complete loss of carbonyl. The reaction mixture was cooled and drowned in 1 liter of water, charged with 400 ml of methylene chloride, and neutralized with HOAc. The organic layer was drawn off, washed with water, and dried over magnesium sulfate. The solvent was removed under reduced pressure, leaving an amber oil.

The above oil was dissolved 100 ml of pet ether. This solution was added to thionyl chloride (23.8 g; 0.2 mole) under argon at 0-5 C. The reaction mixture was warmed to room temperature and stirred for an additional hour. The solvent and excess thionyl chloride were removed under reduced pressure, leaving 48 g of a brown oil. IR indicated that this oil was the desired product.

The above oil was dissolved 200 ml of Isopar-H (Exxon) and charged with quinoline (4 g). The reaction mixture was heated at 135 C. under argon for 36 hr. The solvent was removed under reduced pressure, leaving an oil, which by TLC showed several components. Elution of this oil through the HPLC using cyclohexane afforded 6.7 g of a red oil containing 4 major components by TLC. After eluting this fraction through the HPLC again, a fraction was obtained having only a red and a minor faint blue fluorescent spot. After removal of solvent under reduced pressure, the resulting red oil was dissolved in refluxing methyl cellosolve and cooled slowly, causing the deposition of 1 g of red crystals. TLC of this solid showed only one component. Chemiluminescence in cyclohexane-water emulsion was an intense red.

4',4'''-Bis(n-dodecyl)rubrene (28)

A suspension of p-n-dodecylphenylacetylene (42 g; 0.14 mole), lithium amide (3.2 g; 0.14 mole), and dioxane (75 ml) was stirred under argon for 2 hr at room temperature. Benzophenone (21.8 g; 0.12 mole) was added at room temperature, and the reaction mixture was heated at 100 C. for 18 hr. IR indicated only a slight loss of carbonyl. The reaction mixture was cooled to 40 C., additional p-n-dodecylphenylacetylene (20 g; 0.067 mole) and lithium amide (1.5 g) were added, and the mixture was heated again at 100 C. After 2 hr IR indicated almost complete loss of carbonyl. The reaction mixture was cooled, drowned in water, and made neutral with HOAc. The aqueous mixture was extracted with ether, washed with water, dried over magnesium sulfate, and solvent was evaporated under vacuum to give a dark amber oil, which by TLC was a mixture of the starting material and product. Elution with cyclohexane through the HPLC removed the starting material. Elution with EtOAc gave the carbinol, which by TLC contained only a trace of starting material. Evaporation of the solvent under reduced pressure afforded 47 g of an amber oil which on standing slowly crystallized to a low-melting solid. The IR spectrum was consistent with the expected carbinol.

The carbinol (22.6 g; 0.05 mole) was dissolved in pet ether (125 ml), and thionyl chloride (11.9 g; 0.1 mole) was added during 30 min at -15 C. The reaction mixture was warmed to room temperature and stirred for 1 hr. Solvent and excess thionyl chloride were removed under vacuum, leaving an amber oil whose IR was devoid of hydroxyl absorption.

The above product was dissolved in chlorobenzene (50 ml), quinoline (2 ml) was added, and the mixture was refluxed for 18 hr under argon. The product mixture was cooled, and the solvent was removed under reduced pressure. A red oil was recovered which crystallized on standing. Recrystallization from methyl cellosolve gave 1 g of red crystals, which gave intense red chemiluminescence in cyclohexane-water. TLC showed a single spot on silica (cyclohexane eluent).

3,9,3',3'''-Tetrabromorubrene (29a)

Lithium amide (6.8 g; 0.294 mole) and phenylacetylene (30 g; 0.294 mole) were stirred at room temperature in 100 ml of dioxane. After 1 hr, a slurry of 3,3'-dibromobenzophenone (50 g; 0.147 mole) in 50 ml of dioxane was added. The reaction mixture was stirred for 1 hr at room temperature and heated to 105 C. After 2.5 hr at 105 C. a sample showed complete loss of carbonyl by IR. The reaction mixture was cooled and drowned in 1200 ml of water and neutralized with acetic acid. Methylene chloride (200 ml) was added, and the aqueous layer was separated and washed twice with 100 ml of methylene chloride. The organic layers were combined, and the solvent was removed under reduced pressure, leaving 65 g of a light yellow oil.

The crude carbinol was dissolved in 300 ml of carbon tetrachloride, and the mixture was cooled to -15 C. Thionyl chloride (35 g; 0.294 mole) was added during 30 min at -10 C. The reaction mixture was warmed to room temperature during 2 hr and stirred at room temperature for an additional hour. The IR showed almost

complete loss of the hydroxyl. Solvent and excess thionyl chloride were removed under reduced pressure. Pet ether was added, and the solvent was again removed under reduced pressure at room temperature. This was repeated, and 76 g of a brown oil was obtained.

The crude chloride was dissolved in 25 ml of chlorobenzene, and 1 ml of quinoline was added. The mixture was refluxed for 20 hr, and the solvent was removed under reduced pressure. The resulting red-brown gum was dissolved in 800 ml of refluxing acetonitrile, treated with Darco and Hyflo, and filtered. TLC (silica; cyclohexane) showed a red, a dull green, and a blue spot near the origin under long-wave UV light. A second recrystallization effected no improvement. The entire 10 g sample was eluted with cyclohexane through the HPLC, yielding 3.3 g of a red solid, mp 210-212, which by TLC was a single spot.

Anal. Calcd for C₄₂H₂₄Br₄: C, 59.46; H, 2.86; Br, 37.68.

Found: C, 58.25; H, 3.26; Br, 27.23; Cl, 10.16.

Mass spectrum: m/e 844 (C₄₂H₂₄Br₄), major component; minor components at m/e 800 (C₄₂H₂₄Br₃Cl) and 756 (C₄₂H₂₄Br₂Cl₂).

3,9,4',4'''-Tetrabromorubrene (29b)

Under an argon blanket, phenylacetylene (18 g; 0.176 mole) and lithium amide (4.1 g; 0.176 mole) in 150 ml of dioxane were stirred at room temperature for 1.5 hr. To this slurry, 4,4'-dibromobenzophenone (30 g; 0.088 mole) was added, and the mixture was heated at 100°C. for 16 hr. A sample showed complete loss of carbonyl by IR. The reaction mixture was drowned in 600 ml of water and was made acidic with acetic acid. A yellow oil separated, and the aqueous layer was decanted off. Methylcyclohexane was added to the oil, which solidified after 15 min of stirring. The solid was filtered, and recrystallization from methylcyclohexane gave 33 g (85%) of the product. The IR spectrum was consistent with the expected carbinol, mp 170-172.

The crude carbinol (2 g; 0.0045 mole) was dissolved in 10 ml of petroleum ether, and thionyl chloride (1.1 g; 0.009 mole) was added at 5°C. The reaction mixture was warmed to room temperature and stirred overnight. IR indicated complete loss of the hydroxyl band. Solvent and excess thionyl chloride were removed under reduced pressure, leaving an oil.

Bromobenzene (15 ml) and 2 drops of quinoline were added to the above oil, and the mixture was refluxed under argon. After 16 hr solvent was removed under reduced pressure, leaving a red oil. TLC (silica, cyclohexane eluent) showed 3 components under long-wave UV light; a quencher at Rf=.64, a red fluorescer at Rf=.37, and a dull green at Rf=.17. The sample was dissolved in cyclohexane and eluted through the HPLC on silica. The appropriate fractions were combined, and the solvent was evaporated under vacuum, leaving 0.4 g of a red solid. This solid showed one fluorescent component on TLC at Rf=0.4. Mass spectrum: m/e 844 (C₄₂H₂₄Br₄) major component; minor components at m/e 800 (C₄₂H₂₄Br₃Cl) and m/e 756 (C₄₂H₂₄BrCl₂).

Rubrene sulfonate, sodium salt (3)

Under a blanket of argon, sulfur trioxide (3 ml) was distilled into 50 ml of dry methylene chloride. The gain in weight was equivalent to 4.1 g (0.051 mole) of sulfur trioxide. A slurry of rubrene (10 g; 0.0188 mole) in 250 ml of dry methylene chloride under argon was stirred and cooled in an ice bath. The above solution of SO₃ was added over 1.5 hr and stirred for 1 hr. While still cold, the reaction mixture was drowned into a solution of sodium carbonate (11.7 g; 0.11 mole) in 250 ml of water. The mixture was stirred and heated with an argon bubbler below the liquid surface until the methylene chloride evaporated, then heated to 80 C. This mixture was filtered by gravity through paper, giving 2-3 g of insolubles. The filtrate was evaporated on a steam bath under an argon stream. The dried solid was extracted in a Soxhlet extractor using 300 ml of methanol. The solvent was removed under reduced pressure, leaving 11.3 g of a red solid. TLC showed that a complex mixture was present. Elemental analysis suggested approximately two sulfonate groups per rubrene molecule. Extensive efforts to purify this material by preparative HPLC on reverse-phase C18 silica were unsuccessful. In general, the fractions gave poorer chemiluminescent performance than the mixture itself.

Anal. Found: C, 49.86; H, 3.82; S, 6.14; Na, 6.24.

1-Pyrenylmethyltrimethylammonium methosulfate (22)

A solution of 1-pyrenecarboxaldehyde (11.5 g; 0.05 mole) in DMF (2 g; 0.3 mole) and formic acid (2.75 g; 0.05 mole) was refluxed at 165 C. for 6 hr and stirred at room temperature for an additional 18 hr. The reaction mixture was evaporated to dryness, and the residue was extracted with diethyl ether (3x100 ml) and filtered. Dry, gaseous hydrogen chloride was bubbled through the ether solution for several minutes, and the precipitated amine salt was filtered, washed with ether, and dried in vacuum to give 7.8 g (63%) of the product. This amine salt was suspended in 200 ml of dry ether and neutralized by stirring for 1 hr with 1M aqueous sodium hydroxide (50 ml). The ether layer was separated, dried over anhydrous magnesium sulfate, and concentrated in vacuo to give a viscous oil which solidified upon standing. This solid was extracted with cyclohexane and filtered. Evaporation of the cyclohexane gave 5.92 g of the desired product, mp 53-55 (lit. (44) 54-56).

NMR (CDCl₃): 8.8-8.0 ppm, m, 9H (aromatic); 4.6 ppm, s, 2H; 2.6 ppm, s, 6H.

To a stirred solution of 1-pyrenylmethyldimethylamine (3 g; 0.012 mole) in 60 ml of dry acetone was added dimethylsulfate (15.3 g; 0.12 mole) at 0 C. under a nitrogen atmosphere. A white precipitate formed within 10 min. The mixture was stirred for 1 hr and filtered. The solid was collected and dried under vacuum; yield 3.5 g (65%), mp 134-136.

Anal. Calcd for C₂₁H₂₃N₀4S: C, 65.45; H, 5.97; N, 3.64.
Found: C, 65.23; H, 6.24; N, 3.49.

NMR (DMSO-d₆): 8.4 ppm, m, 9H; 5.4 ppm, s, 2H; 3.6 ppm, s, 3H; 3.3 ppm, s, 9H.

1-Pyrenylbutanoyl chloride (118)

4-(1'-Pyrene)butyric acid (2.1 g; 0.0097 mole) suspended in 50 ml of dry benzene was added dropwise to a solution of oxalyl chloride (3.1 g; 0.024 mole) in 10 ml of benzene at room temperature under a nitrogen atmosphere. After the addition was complete, the mixture was heated to 75 C. and held for 2 hr. Evaporation of the solvent gave 2.67 g (90%) of a light yellow solid. It was recrystallized from cyclohexane, mp 62-64 C.
Anal. Calcd for C₂₀H₁₅OCl: C, 78.30; H, 4.89.
 Found: C, 78.57; H, 4.89.

2-(N-morpholinyl)ethyl-4'-(1''-pyrenyl) butyrate (99)

1-Pyrenebutanoyl chloride (2 g; 0.0065 mole) was added in portions to a solution of N-2-hydroxyethylmorpholine (0.95 g; 0.0065 mole) and triethylamine (0.8 g; 0.0079 mole) in 50 ml of benzene at room temperature under a nitrogen atmosphere. The mixture was heated at reflux for 3 hr, then held at room temperature for 18 hr. The precipitated triethylamine hydrochloride (0.8 g) was removed by filtration, and the solvent was evaporated from the filtrate, affording 3.0 g of an oil whose NMR and IR spectra were consistent with the expected structure.
 NMR (CDCl₃): 8.0 ppm, m, 9H; 4.2 ppm, t, 2H; 3.65 ppm, m, 4H; 3.4 ppm, t, 2H; 2.5 ppm, m, 10H.
 IR (methylene chloride): 1720, 1600, 1440, and 1260.

2-(N-methylmorpholinium)ethyl-4'-(1''-pyrenyl) butyrate, methosulfate (21)

To a solution of the amine 119 (2.64; 0.006 mole) in 50 ml of dry acetone was added 8 g (0.063 mole) of dimethylsulfate at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was heated to 50 C. and held there for 1.5 hr. The white solid was isolated by filtration and dried under vacuum to give 2.28 g (72%) of the quaternary ammonium salt, mp 115-117 .
Anal. Calcd for C₂₈H₃₂N₀7S: C, 63.88; H, 6.08; N, 2.66.
 Found: C, 63.27; H, 6.26; N, 2.38.
 NMR (DMSO-d₆): 3.2 ppm, m, 9H; 4.50 ppm, broad s, 2H; 3.9 ppm, broad s, 5H; 3.40 ppm, m, 9H; 3.20 ppm, s, 4H; 2.50 ppm, m, 4H.
 IR (Nujol): 1740, 1440, 1370, 1240, 1120, and 1150.

4-(1'-Pyrenyl)butanoic acid, sodium salt (8)

To a solution of sodium hydroxide (0.4 g; 0.01 mole) in 50 ml of water was added 4-(1'-pyrenyl)butyric acid (2.88 g; 0.01 mole). The mixture was stirred while warming on a hot plate until all the acid was dissolved. The solution was filtered and the filtrate evaporated to dryness to give 3.48 g of the crude solid product. Recrystallization from ethanol afforded the salt, mp >260.
Anal. Calcd for C₂₀H₁₅O₂Na: C, 77.42; H, 4.84.
 Found: C, 77.2; H, 4.98.
 IR (Nujol): 1720, 1660, 1540, 1370, and 1220.

3-(Trimethylammonium)-6-(dimethylamino)acridine triflate (121)

3,6-Bis-(dimethylamino)acridine hydrochloride (Acridine Orange)(5.0 g; 0.0166 mole) was dissolved in 100 ml of water. The solution was filtered and made basic with 5N sodium hydroxide. The resulting solid product was filtered, air-dried, and recrystallized from 400 ml of methylcyclohexane to give 2.6 g (59%) of 3,6-bis-(dimethylamino)-acridine, mp 182-183, lit. (41) mp 181.

3,6-Bis-(dimethylamino)-acridine (0.5 g; 0.00189 mole) was dissolved in 25 ml of methylene chloride, and methyl triflate (1.0 g) was added dropwise. The reaction mixture was stirred for 30 min; the product was filtered, washed with 10 ml of methylene chloride, and dried under vacuum at room temperature. The yield of the quaternary ammonium salt was 0.7 g (86%), mp 310-311, dec.; the product was analytically pure without recrystallization.
Anal. Calcd for C₁₉ H₂₂ F₃ N₃ O₃ S: C, 53.15; H, 5.13; N, 9.79. Found: C, 52.69; H, 5.10; N, 9.92.

2,4-Dichloro-6-sulfophenol, tetramethylammonium salt, oxalate ester (158)

Hydrolysis of 2-hydroxy-3,5-dichlorobenzenesulfonyl chloride (13.1 g; 0.05 mole) was accomplished by refluxing with 50 ml of distilled water with stirring for 30 min. The hot solution was filtered, and evaporation of the solvent from the filtrate yielded a yellow residue. The sulfonic acid was neutralized by the addition of a 20% solution of tetramethylammonium hydroxide in methanol, yielding a clear solution. Evaporation of the solvent left a sticky, slightly pink solid (45.7 g) which was washed two times with dichloromethane. This solid was recrystallized from 50 ml of acetonitrile, yielding a white crystalline solid (20.8 g), which was washed twice with acetonitrile and once with dichloromethane. NMR indicated that a small amount of acetonitrile remained in the sample. It was used without purification in the following step.

The tetramethylammonium salt prepared above (15.0 g; 0.05 mole) was added to 400 ml of dichloromethane, and to this mixture was added triethylamine (6.94 ml, 0.05 mole). A solution of oxalyl chloride (2.13 ml, 0.025 mole) in 10 ml of dichloromethane was added during 10 to 15 min. The mixture was then heated at reflux for 30 min, cooled to room temperature, filtered, and washed two times with dichloromethane. Air drying afforded an off-white solid (14.4 g), mp 272-277, dec, gas evolution. An attempt to purify this material by recrystallization from DMSO gave a solid, mp 294-296, dec, whose elemental analysis was unsatisfactory.
Anal. Calcd for C₂₂ H₂₈ Cl₄ S₂ N₂ O₁₀: C, 38.49; H, 4.35; Cl, 20.66; S, 11.25; N, 3.64.
Found: C, 37.19; H, 4.35; Cl, 18.72; S, 11.25; N, 3.64.

A qualitative chemiluminescent test on this material in aqueous solution with hydrogen peroxide and 8-hydroxy-1,3,6-pyrene trisulfonate was very weak and short-lived.

2,4,5-Trichloro-6-sulfophenol, tetramethylammonium salt, oxalate ester (160)

To chlorosulfonic acid (67 ml; 1.0 mole) at room temperature was added 39.5 g (0.20 mole) of 2,4,5-trichlorophenol in several portions. Vigorous gas evolution was evident after each addition of the solid. The temperature of the reaction mixture dropped to 10 C., and the mixture solidified. An additional 20 ml of chlorosulfonic acid was added, and the mixture was warmed to room temperature to dissolve the solid. The reaction mixture was then heated to 95 C. during 3 hr, held at 95 C. for 6 hr, and allowed to cool to room temperature overnight. The mixture was then carefully quenched onto cracked ice (very violent reaction), and the aqueous mixture was extracted with 400 ml of chloroform. Evaporation of the solvent under reduced pressure gave a liquid-solid mixture which solidified on addition of cyclohexane. Filtration afforded a tan solid (11.3 g). IR of this solid showed the expected sulfonyl chloride bands at 1420 and 1195 cm⁻¹. NMR showed a strong aromatic singlet at 7.6 ppm and small amounts of impurities at 8.0 and 1.3 ppm. A second crop was obtained from the cyclohexane filtrate from the sulfonyl chloride, but it appeared to be less pure and was discarded. The crude sulfonyl chloride (8.5 g) was hydrolyzed in 150 ml of water by boiling for 2.5 hr. The solution was filtered, and solvent was evaporated from the filtrate under reduced pressure, leaving a colorless oil which solidified on standing overnight. The crude 2-hydroxy-3,5,6-trichlorobenzenesulfonic acid (8.5 g) was neutralized to pH 3.5 in aqueous solution with 20% tetramethylammonium hydroxide in methanol. Evaporation of the solvent under reduced pressure and recrystallization from water with charcoal decolorization afforded two crops of the salt which were combined, yield 11.9 g, mp 274-7. NMR indicated some water was present in this sample. Drying under vacuum at 80 C. removed the water and afforded the anhydrous salt. Recrystallization of the salt from acetone afforded the analytically pure material, mp 286-9.

Anal. Calcd for C₁₀H₁₄N₁S C₁₃O₄: C, 34.25; H, 4.02; N, 3.99; S, 9.14; Cl, 30.33.

Found: C, 34.52; H, 4.00; N, 3.86; S, 8.94; Cl, 28.93.

IR (Nujol): 1260, 1170, 1120, 1020, 950, 670, and 610.

NMR (DMSO-d₆): 3.2 ppm, 12H; 7.8 ppm, 1H; 12.7 ppm, 1H (exchanged with D₂O).

The tetramethylammonium salt (6.69 g; 0.02 mole) was slurried with 50 ml of dichloromethane along with triethylamine (2.78 ml; 0.02 mole). Oxalyl chloride (0.85 ml; 0.01 mole) was added dropwise during 5 min. An additional 25 ml of solvent was added at this point to fluidize the reaction mixture. After stirring overnight at ambient temperature, a tan solid was filtered, washed with dichloromethane, and air-dried on the filter to yield 6.22 g of the crude oxalate ester. An attempt to purify this salt by recrystallization from a number of different solvents was unsuccessful. A solid (mp 294-6) was obtained from DMSO, but elemental analysis was unsatisfactory.

Anal. Calcd for C₂₂H₂₈N₂C₁₆S₂O₁₀: C, 34.98; H, 3.47; N, 3.71; Cl, 28.16; S, 8.49.

Found: C, 37.19; H, 4.35; N, 3.64; Cl, 18.72; S, 11.25.

Treatment of an aqueous solution of this solid with hydrogen peroxide in the presence of 8-hydroxy-1,3,6-pyrene trisulfonate gave only a weak emission with a very short lifetime.
N-(2-Morpholinoethyl)trifluoromethanesulfonamide (123)

Trifluoromethanesulfonic anhydride (40.46 g; 0.143 mole) was added dropwise to a stirred solution of N-(2-aminoethyl)morpholine (37.34 g; 0.286 mole) in methylene chloride (200 ml) at 0 C. under a nitrogen atmosphere. When the addition was completed the mixture was stirred at room temperature for 3 hr. The white precipitate was separated by filtration, and the filtrate was evaporated to obtain 47.31 g of the crude product. Recrystallization of this crude product from cyclohexane gave the desired product (32.56 g), mp 106-108.

Anal. Calcd for C₇H₁₃N₂O₃S F₃: C, 32.06; H, 4.96; N, 10.69; S, 12.21; F, 21.76.

Found: C, 32.08; H, 4.87; N, 10.54; S, 12.02; F, 21.50.
 IR (methylene chloride): 3300, 1360, 1195, and 1140.

N,N'-Bis(2-morpholinoethyl)-N,N'-bis(trifluoromethylsulfonyl)oxamide (31, METO)

Oxalyl chloride (11.10 g; 0.076 mole) was added dropwise to a solution of the triflylamide 1 (37.72 g; 0.152 mole) and triethyl amine (15.39 g; 0.153 mole) in dry THF (400 ml) at 0 C. under a nitrogen atmosphere during a period of 90 min. After the addition was completed, the mixture was stirred at room temperature for 4 hr and filtered. The filtrate was concentrated to remove THF and filtered to give 34.36 g of the crude product. Recrystallization of this crude product from petroleum ether gave the desired product, mp 62-64.

Anal. Calcd for C₁₆H₂₄N₄O₈S₂F₆: C, 33.32; H, 4.18; N, 9.69; S, 11.08; F, 19.71.

Found: C, 33.49; H, 4.29; N, 9.74; S, 10.86; F, 19.45.
 IR (Nujol): 1740, 1720, 1370, 1200, 1160 and 1120.

4,4'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]ethylene-bis-(N-methylmorpholinium) trifluoromethanesulfonate (4, METQ)

Methyl trifluoromethanesulfonate (7.25 g; 0.044 mole) was added portionwise to a solution of triflyloxamide 4 (10 g; 0.0174 mole) in methylene chloride (50 ml) at 0 C. under a nitrogen atmosphere. After the solution was completed, the mixture was stirred at room temperature for 20 hr. The white precipitate was separated by filtration and washed several times with methylene chloride. After drying under vacuum, the product (14.3 g) had mp 160-165.

Anal. Calcd for C₂₀H₃₀N₄O₁₄S₄F₁₂: C, 26.49; H, 3.31; N, 6.18.
 Found: C, 26.20; H, 3.44; N, 6.55.

IR (Nujol): 1740, 1720, 1380, 1220, and 1160.

N-[2-(2'-Pyridyl)ethyl]trifluoromethanesulfonamide

Trifluoromethanesulfonic anhydride (11.74 g; 0.042 mole) was added dropwise to a stirred solution of 2-(2'-aminoethyl)pyridine (10 g; 0.82 mole) in methylene chloride (8 ml) at 0 C. under a

nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 2 hr. The brown methylene chloride solution was evaporated to give 8.01 g of the crude solid product. Recrystallization of this crude product from methylcyclohexane gave the pure triflylamide, mp 83-85.
Anal. Calcd for C₈ H₉ N₂ O₂ S F₃: C, 37.79; H, 3.54; N, 11.02.
Found: C, 37.73; H, 3.58; N, 10.96.
Mass Spectrum (CI): m/e 255 (M + H).

N,N'-Bis[2-(2'-pyridyl)ethyl]N,N'-bis(trifluoromethylsulfonyl)oxamide

To a stirred solution of the above triflylamide (7.5 g; 0.03 mole) and triethylamine (4 g; 0.04 mole) in 120 ml of dry THF was added very slowly a solution of oxalyl chloride (2.2 g; 0.0172 mole) in 30 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 2 hr. The light brown reaction mixture was filtered to separate the solid crude product. Recrystallization of this crude product from cyclohexane gave the pure oxamide (5.69g), mp 136-138.
Anal. Calcd for C₁₈ H₁₆ N₄ O₆ S₂ F₆: C, 38.43; H, 2.85; N, 9.96.
Found: C, 38.92; H, 3.01; N, 10.05.
IR (Nujol): 1740, 1720, 1360, 1200, and 1160.

2,2'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]ethylene-bis(N-methyl-pyridinium) trifluoromethanesulfonate (1, PETQ)

Methyl trifluoromethanesulfonate (0.72 g; 0.004 mole) was added in portions to a solution of the above triflyloxamide (0.5 g, 0.0009 mole) in methylene chloride (30 ml) at 0 C. under a nitrogen atmosphere. After the addition was completed, the reaction mixture was stirred at room temperature for 2 hr. The white solid was separated by filtration and washed with methylene chloride to obtain the desired product, mp 173-178.
Anal. Calcd for C₂₂ H₂₂ N₄ O₁₁ S₃ F₁₂: C, 29.66; H, 2.47; N, 6.69.
Found: C, 29.89; H, 2.30, N, 6.48.

4,4'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]ethylene-bis(morpholinium) chloride (124, METH)

Into a stirred solution of N,N'-bis(2-morpholinoethyl)-N,N'-bis trifluoromethylsulfonyl)oxamide 31 (2.5 g; 0.0043 mole) in 80 ml of dry THF was slowly passed a stream of hydrogen chloride gas at room temperature for 15 min. The mixture, containing a white solid, was evaporated to dryness and stirred with 100 ml of ether. The white solid which remained was separated by filtration and dried in vacuum (2.4 g), mp 140-143.

Anal. Calcd for C₁₆ H₂₆ N₄ O₈ S₂ C₁₂ F₆: C, 29.49; H, 3.99; N, 8.60.
Found: C, 29.71; H, 3.65; N, 8.38.
IR (Nujol): 3400, 2600, 2500, 2350, 1740, 1720, 1370, 1220 and 1170.

2,2'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]ethylene-bis(pyridinium) chloride (2, PETH)

To a solution of N-[2-(2'-pyridyl)ethyl]trifluoromethanesulfonamide (19.17 g; 0.0755 mole) and 4-dimethylaminopyridine (9.3 g; 0.076 mole) in 100 ml of dry THF was added dropwise a solution of oxalyl chloride (10.62 g; 0.084 mole) in 20 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 3 hr. The white solid was isolated by filtration and stirred with methylene chloride. The solid (26.83 g) that remained was separated by filtration and recrystallized from acetonitrile-water to give the pure compound, mp 179-184, dec.

Anal. Calcd for C₁₈ H₁₈ N₄ O₆ S₂ F₈ C₁₂: C, 34.02; H, 2.83; N, 8.82.

Found: C, 34.11; H, 2.87; N, 8.67.

IR (Nujol): 3400, 2350, 2080, 2010, 1720, 1370, 1220, and 1140.

N-(3-Morpholinopropyl)trifluoromethanesulfonamide

Trifluoromethanesulfonic anhydride (20.12 g; 0.07 mole) was added dropwise to a stirred solution of N-(3-aminopropyl)morpholine (20 g; 0.14 mole) in methylene chloride (50 ml) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 3 hr. Evaporation of the solvent gave 43.29 g of oil which was stirred with hot toluene. The toluene layer was separated and evaporated to give 15.97 g of the crude triflylamide. It was recrystallized from methylcyclohexane, mp 95-97.

Anal. Calcd for C₈ H₁₅ N₂ O₃ S F₃: C, 35.29. H, 5.51; N, 10.29.

Found: C, 35.33; H, 5.52; N, 10.05.

N,N'-Bis(3-morpholinopropyl)-N,N'-bis-(trifluoromethylsulfonyl)oxamide

Oxalyl chloride (2.33 g; 0.018 mole) in 10 ml of dry THF was added dropwise to a solution of the above triflylamide (7.5 g; 0.029 mole) and triethylamine (2.9 g; 0.029 mole) in 70 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 3 hr. Evaporation of the solvent gave 12.97 g of solid which was stirred with hot toluene. The solid that remained was isolated by filtration. Evaporation of toluene gave 6 g of a semi-solid which was recrystallized from toluene-cyclohexane to give the pure oxamide, mp 112-114.

Anal. Calcd for C₁₈ H₂₈ N₄ S₂ O₈ F₆: C, 35.64; H, 4.62; N, 9.24.

Found: C, 36.22; H, 4.68; N, 9.12.

4,4'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]trimethylene-bis-(morpholinium) chloride (125)

The toluene-insoluble solid from the preparation of the oxamide above was stirred with methylene chloride to remove triethylamine hydrochloride. The solid that remained was isolated by filtration and recrystallized from acetonitrile to give pure 107, mp 171-173.

Anal. Calcd for C₁₈ H₃₀ N₄ S₂ O₆ C₁₂ F₆: C, 33.38; H, 4.64; N, 8.66.

Found: C, 33.07; H, 4.74; N, 8.40.

4,4'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]trimethylene-bis-(4-methylmorpholinium) trifluoromethanesulfonate (6, MPTQ)

Methyl trifluoromethanesulfonate (2.18 g; 0.013 mole) was added in portions to a solution of N,N'-bis(3-morpholinopropyl)-N,N'-bis(trifluoromethylsulfonyl)oxamide (1.5 g; 0.0026 mole) in methylene chloride (50 ml) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 2 hr. The white solid was separated by filtration and washed with methylene chloride to give the desired product, mp 148-150.

Anal. Calcd for C₂₂H₃₄N₄O₁₄S₄F₁₂: C, 28.27; H, 3.64; N, 6.00. Found: C, 28.33; H, 3.64; N, 5.78.

N-(N'-benzyl)-4-piperidinyl-trifluoromethanesulfonamide

Trifluoromethanesulfonic anhydride (18.45 g; 0.065 mole) was added dropwise to a stirred solution of 4-amino-1-benzylpiperidine (25 g; 0.13 mole) in methylene chloride (100 ml) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature overnight. The white precipitate was isolated by filtration, yield 29.5 g. Evaporation of the filtrate gave 15.83 g of yellow crude solid product. It was recrystallized from cyclohexane, mp 124-126.

IR (methylene chloride): 3350, 1370, 1195, and 1140.
Mass spectrum: m/e 322 (M⁺).

N,N-Bis[(1-benzyl)-4-piperidinyl]-N,N'-bis[(trifluoromethyl)sulfonyl]oxamide

Oxalyl chloride (1.45 g; 0.012 mole) in 10 ml of dry THF was added dropwise to a stirred solution of the above triflylamide (6.42 g; 0.02 mole) and triethylamine (2.1 g; 0.12 mole) in 50 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 3 hr. The white precipitate was separated by filtration. Evaporation of the THF filtrate gave 6.3 g of the crude product which was recrystallized from hexane, mp 130-133.

IR (methylene chloride): 1710, 1410, 1360, 1220 and 1140.
Anal. Calcd for C₂₈H₃₀N₄O₆S₂F₆: C, 48.28; H, 4.31; N, 8.05. Found: C, 47.72; H, 4.6; N, 8.08.

4,4'-Oxalyl-bis[(trifluoromethylsulfonyl)imino]ethylene-bis-(1-methyl-1-benzylpiperidinium) trifluoromethanesulfonate (9, BPTQ)

Methyl trifluoromethanesulfonate (2.18 g; 0.0133 mole) was added in portions to a solution of the above triflyloxamide (1.5 g; 0.0022 mole) in 30 ml of methylene chloride at room temperature. After the addition was completed, the mixture was stirred overnight. The oily precipitate was separated from methylene chloride and was stirred with diethyl ether. The white solid thus formed was isolated by filtration and dried under vacuum (1.8 g), mp 125-130.
IR (Nujol): 3400, 1710, 1360, 1220, and 1140.

N-(2-Pyridylmethyl)trifluoromethanesulfonamide

Trifluoromethanesulfonic anhydride (14.1 g; 0.05 mole) was added dropwise to a solution of 2-aminomethylpyridine (10.4 g; 0.096 mole) in 100 ml of methylene chloride at 0 C. under a nitrogen atmosphere. After the addition was complete, the mixture was stirred at room temperature for 3 hr, and the yellow solid was isolated by filtration (14.96 g). Evaporation of the filtrate gave 9.40 g of brown solid, which was extracted with ether. Evaporation of the ether layer gave 7.57 g of the crude yellow product. Recrystallization of this crude product from cyclohexane-ether gave the pure compound, mp 93-95.

IR (Nujol): 3150, 1370, 1260, and 1150.

Anal. Calcd for C₇H₇N₂O₂F₃: C, 35.00; H, 2.92; N, 11.67. Found: C, 35.35; H, 2.93; N, 12.10.

Attempted preparation of N,N'-bis(2-pyridylmethyl)-N,N'-bis-(trifluoromethylsulfonyl) oxamide (127)

To a solution of N-(2-pyridylmethyl)trifluoromethanesulfonamide (2.4 g; 0.01 mole) and triethylamine (1.1 g; 0.011 mole) in 50 ml of THF was added dropwise a solution of oxalyl chloride (0.87 g; 0.007 mole) in 5 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was filtered, and the THF filtrate was evaporated to give 2.24 g of a dark semi-solid which was extracted with ether. However, evaporation of ether gave only a trace amount of material. The ether-insoluble material appeared to be polymeric.

N-[(Trifluoromethyl)sulfonyl]glycine ethyl ester

To a suspension of glycine ethyl ester hydrochloride (69.0 g; 0.49 mole) in triethylamine (120 g; 1.17 mole) and methylene chloride (500 ml) was added dropwise trifluoromethanesulfonic anhydride (164 g; 0.58 mole) at 0 C. under a nitrogen atmosphere. The mixture was stirred at room temperature for 20 hr. Filtration of the mixture gave 5.1 g of the unreacted glycine ethyl ester hydrochloride. Evaporation of the methylene chloride filtrate gave 308.1 g of a semi-solid, which was stirred with diethyl ether (3 X 400 ml). Evaporation of the ether layer gave 67.87 g of the crude product. It was recrystallized from cyclohexane, mp 73-75.

Anal. Calcd for C₅H₈N₀4S F₃: C, 25.55; H, 3.40; N, 5.96.

Found: C, 25.77; H, 3.70; N, 5.96

IR (Nujol): 3225, 1720, 1370, 1200, and 1150.

NMR (acetone-d₆): 4.8 ppm, t, 3H; 4.2 ppm, q, 2H; 4.1 ppm, s, 2H and 1.1 ppm, t, 3H.

Mass spectrum: m/e 235 (M⁺).

N,N'-Oxalyl-bis[N-(trifluoromethylsulfonyl)glycine] diethyl ester (130)

To a solution of the above triflylamide (6.2 g; 0.026 mole) in 2.7 g (0.027 mole) of triethylamine and 50 ml of dry tetrahydrofuran (THF) was added dropwise a solution of oxalyl chloride (2.18 g; 0.017 mole) in dry THF (20 ml) at 0 C. under a nitrogen atmosphere. The mixture was stirred at room temperature for 3 hr. Filtration of the mixture gave 3.7 g of solid triethylamine hydrochloride. The

filtrate was evaporated to give 6.88 g of the crude product. Recrystallization of this crude product from cyclohexane gave the pure compound, mp 88-90.

Anal. Calcd for C₁₂H₁₀N₂O₁₀S₂F₆: C, 27.48; H, 2.67; N, 5.34.

Found: 27.69; H, 2.74; N, 5.21.

IR (Nujol): 3400, 1720, 1370, 1220, and 1160.

Mass spectrum (CI): m/e 525 (M+H).

N-[(Trifluoromethyl)sulfonyl]glycine benzyl ester

Glycine benzyl ester hydrochloride was prepared according to a literature procedure. To the suspension of glycine benzyl ester hydrochloride (11 g; 0.055 mole) in 120 ml of methylene chloride containing 11 g (0.112 mole) of triethylamine was added dropwise a solution of trifluoromethanesulfonic anhydride (15.6 g; 0.055 mole) in 20 ml of methylene chloride at 0 C. under a nitrogen atmosphere. After the addition was complete the mixture was stirred at room temperature for 3 hr. Evaporation of the reaction mixture gave 35.99 g of an oil which was extracted with ether on a steam bath. The ether layer was separated and evaporated to give 7.36 g of the crude product. It was recrystallized from toluene-cyclohexane, mp 78-81.

Mass spectrum, m/e 281 (M+).

IR (nujol): 3200, 1720, 1370, 1180, and 1140.

N,N'-Oxalyl-bis[N-(trifluoromethylsulfonyl)glycine] dibenzyl ester (131)

To a solution of the above triflylamide (7.09 g; 0.025 mole) in 80 ml of THF containing 3 g (0.03 mole) of triethylamine was added dropwise a solution of oxalyl chloride (1.89 g; 0.015 mole) in 20 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for 4 hr. The white solid (4.08 g) from the reaction mixture was isolated by filtration. Evaporation of the THF filtrate gave 8.12 g of an oil which was extracted with cyclohexane on a steam bath. The cyclohexane layer was separated and evaporated to give 6 g of the crude product. It was recrystallized from cyclohexane-hexane, mp 53-55.

Anal. Calcd for C₂₂H₁₈O₁₀N₂F₆S₂: C, 40.74; H, 2.78; N, 4.32.

Found: C, 40.47; H, 2.37; N, 4.47.

IR (CH₂C₁₂): 1740, 1720, 1350, 1170, and 1130.

N-[(Trifluoromethyl)sulfonyl]glycine (133)

(A) A solution of 3.2 g (0.005 mole) of the triflyloxamide 131 in 150 ml of absolute ethanol was hydrogenated over 0.5 g of 10% Pd/C in a Parr shaker hydrogenator at an initial pressure of 36 psi. The hydrogenation was continued for 24 hr at 40 C. After being cooled to room temperature the reaction mixture was filtered and washed with ethanol. Evaporation of the ethanol filtrate gave 2.27 g of a white solid product, which upon drying in vacuum melted at 86-88 C.

Anal. Calcd for C₃H₄N₂O₄S F₃: C, 17.39; H, 1.93; N, 6.76.

Found: C, 17.59; H, 2.01; N, 6.92.

IR (Nujol): 3300, 1710, 1360, 1200, and 1140.

NMR (DMSO-d₆): 3.9 ppm, s, 2H; 9.2 ppm, broad s, 2H, exchanged with

D20.

(B) The ethyl ester of N-[(Trifluoromethyl)sulfonyl]glycine (17.73 g; 0.075 mole) suspended in 150 ml of dilute hydrochloric acid was heated on steam bath (80 C.) for 2 hr. After filtration of the aqueous solution, water was evaporated from the filtrate to give 15.34 g of a solid which upon recrystallization from toluene melted at 90-92 . Its IR and NMR spectra are identical to those of the compound obtained by procedure (A).

N-[(Trifluoromethyl)sulfonyl]glycyl chloride (134)

To N-[(trifluoromethyl)sulfonyl]glycine 133 (8.61 g; 0.04 mole) suspended in 100 ml of thionyl chloride was added 4 drops of pyridine at room temperature under a nitrogen atmosphere. The mixture was heated with stirring at 55 C. for 3 hr. Excess thionyl chloride was evaporated to give a light oil. This oil was treated with diethyl ether, and a small amount of white precipitate was separated by filtration. Evaporation of ether from the filtrate gave 9.20 g of a light yellow liquid.

IR (Neat): 3300, 1795, 1440, 1370, 1200, and 1140.

N-[(Trifluoromethyl)sulfonyl]glycine, 2-(4-morpholinyl)ethyl ester (135)

To N-[(Trifluoromethyl)sulfonyl]glycine 133, (5.0 g; 0.024 mole) in 100 ml of methylene chloride in a three-neck flask were added in sequence N-hydroxyethylmorpholine (3.27 g; 0.026 mole), and 4-pyrrolidinopyridine (30 mg; 0.0002 mole) at room temperature under a nitrogen atmosphere. After the addition, the mixture was stirred overnight at room temperature. The urea was filtered off and washed with methylene chloride. The weight of the solid was 5.0 g. Evaporation of the methylene chloride filtrate gave 8.62 g of an oil, which was treated with diethyl ether-petroleum ether. The white solid that precipitated was isolated by filtration (wt, 6.44 g). Recrystallization of this solid from toluene gave the desired product, mp 94-97.

Mass spectrum: m/e 320.

NMR: 2.5 ppm, m, 6H; 3.5 ppm, m, 4H; 3.95 ppm, s, 2H; 4.15 ppm, t, 2H; 8.1 ppm, s, 1H (NH).

Attempted preparation of N,N'-Oxalyl-bis[N-(trifluoromethylsulfonyl)-glycine] 2-(4-morpholinyl)ethyl ester (136)

To a solution of the triflylamide 135 (2.0 g; 0.0063 mole) in 50 ml of THF containing 0.75 g of triethylamine (0.0075 mole) was added dropwise a solution of oxalyl chloride (0.58 g; 0.0046 mole) in 10 ml of THF at 0 C. under a nitrogen atmosphere. After the addition the mixture was stirred at room temperature for 3 hr. The white solid was separated by filtration (weight of the solid, 0.9 g). Evaporation of the THF filtrate gave 2.07 g of a semi-solid. The IR spectrum of this semi-solid showed a strong carbonyl band at 1750. However, this material did not give chemiluminescence when treated with the fluorescer CBPEA and the standard activator solution (i.e., H₂O₂ and sodium salicylate in dibutyl phthalate). Attempts to purify

this semi-solid were unsuccessful.

N-[(Trifluoromethyl)sulfonyl]glycine 3,6,9,12,15-pentaoxahexadecyl ester

N-[(Trifluoromethyl)sulfonyl]glycyl chloride (135, 2.25 g; 0.01 mole) in 10 ml of dry THF was added dropwise to a solution of 3,6,9,12,15-pentaoxahexadecanol (2.52 g; 0.01 mole) and triethylamine (1.2 g; 0.012 mole) in 50 ml of dry THF at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 2 hr. The white solid precipitate (triethylamine hydrochloride, 1.1g) was isolated by filtration. Evaporation of the THF filtrate gave 4.78 g of an oil. The IR spectrum (3450, 1750, 1380, 1200, and 1150) of this oil indicated the expected triflylamide. However, attempts to purify this oil were unsuccessful.

N,N'-Oxalyl-bis[N-(trifluoromethylsulfonyl)glycine] 3,6,9,12,15-pentaoxahexadecyl ester (137)

Oxalyl chloride (0.58 g; 0.0046 mole) in 10 ml of dry THF was added dropwise to the 3,6,9,12,15-pentaoxahexadecyl ester of N-[(trifluoromethyl)sulfonyl]glycine (3.31 g; 0.0075 mole) and triethylamine (0.9 g; 0.009 mole) in 50 ml of dry THF at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 2 hr. The white solid (1.2 g) was isolated by filtration. Evaporation of THF gave 3.34 g of an oil. Its IR spectrum (1790) indicated the desired product, plus the starting triflylamide. Attempts to purify the product were unsuccessful.

1,1,1-Trifluoro-N-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]methanesulfonamide, (138)

N-[(Trifluoromethyl)sulfonyl]glycyl chloride (134, 5.49 g; 0.024 mole) in 20 ml of dry THF was added dropwise to a solution of N-methylpiperazine (5.14 g; 0.05 mole) in dry THF (50 ml) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature overnight. The solid was isolated by filtration (6.58 g) and was stirred with 100 ml of water. The solid that remained undissolved was isolated by filtration and dried under vacuum to give the pure product (2.80 g).

Anal. Calcd for C₈H₁₄N₃O₃S F₃: C, 33.22; H, 4.84; N, 14.53. Found: C, 33.53; H, 4.92; N, 14.43.

IR: 1200 and 1150.

NMR (CDCl₃): 2.3 ppm, s, 3H; 2.45 ppm, m, 4H; 3.4 ppm, m, 4H; 4.05 ppm, s, 2H; 6.6 ppm, s, 1H (NH).

The original THF filtrate from the reaction mixture was stirred with diethyl ether. Isolation of the precipitate from ether gave an additional 0.75 g of the desired product.

N,N'-Oxalyl-bis[1,1,1-trifluoro-N[2-(4-methyl-1-piperazinyl)2-oxoethyl]methanesulfonamide (129)

Oxalyl chloride (0.44 g; 0.0034 mole) in 10 ml of dry THF was added dropwise to a suspension of the triflyl amide 138 (1.5 g; 0.0052 mole) in 50 ml of THF containing triethylamine (0.5 g; 0.005 mole) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at ice temperature for 2 hr. The hygroscopic white solid (3.0 g) was isolated by filtration. Evaporation of the THF filtrate gave 0.75 g of light yellow solid. Both solids showed strong chemiluminescence in the organic and aqueous systems. However, attempts to purify the product were unsuccessful.

N-(2-Chloro-3-pyridyl)trifluoromethanesulfonamide

To a suspension of 2-chloro-3-aminopyridine (5.14 g; 0.04 mole) and powdered 3A molecular sieves (10 g) in methylene chloride (60 ml) was added dropwise trifluoromethanesulfonic anhydride (5.7 g; 0.02 mole) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 5 hr, and the solid was filtered. The filtrate was evaporated and treated with water to give 5.0 g of the crude solid product. Recrystallization from cyclohexane gave the pure triflyl amide, mp 120-122.
Anal. Calcd for C₆H₄N₂O₂S Cl F₃: C, 27.69; H, 1.54; N, 10.77; S, 12.31.
 Found: C, 27.85; H, 1.41; N, 11.00; S, 11.95.
 IR (CH₂Cl₂): 3300, 1370, 1230, 1210, and 1140.
 NMR (CDCl₃): 7.35 ppm, m, 1H; 8.0 ppm, 2d, 1H; 8.35 ppm, 2d, 1H; 8.30 ppm, s, 1H (NH).
 Mass spectrum: m/e 260 (M⁺).

N,N'-Bis(2-chloro-3-pyridyl)-N,N'-bis(trifluoromethylsulfonyl)-oxamide (140)

Oxalyl chloride (0.77 g; 0.006 mole) was added dropwise into a stirred suspension of N-(2-chloro-3-pyridyl)trifluoromethanesulfonamide (2.61 g; 0.01 mole) and powdered 3A molecular sieves (5.0 g) in methylene chloride (75 ml) at 0 C. under a nitrogen atmosphere. The mixture was heated to 60 C. and held there for 3 hr. The reaction mixture was filtered, and the filtrate was evaporated to dryness. The resulting residue was extracted with diethyl ether, and the combined ethereal extracts were dried over sodium sulfate. Evaporation of the dried ether solution gave 2.33 g of the crude product. It was recrystallized from cyclohexane, m.p. 104-106.
Anal. Calcd for C₁₄H₆N₂O₆S₂Cl₂F₆: C, 29.27; H, 1.05; N, 9.76; S, 11.15.
 Found: C, 29.10; H, 1.14; N, 9.90; S, 10.89.
 IR (CH₂Cl₂): 1750, 1730, 1420, 1360, 1220, and 1130.
 NMR (CDCl₃): 7.50 ppm, m, 1H; 8.10 ppm, 2d, 1H, J=4Hz; 8.5 ppm, m, 1H.
 Mass spectrum: m/e 574 (M⁺).

N-(4-Chloro-3-pyridyl)trifluoromethanesulfonamide

To a solution of 5-amino-2-chloropyridine (10 g; 0.078 mole) in 100 ml of methylene chloride was added dropwise trifluormethanesulfonic anhydride (11.74 g; 0.04 mole) at 0 C. under a nitrogen atmosphere. After the addition was completed, the mixture was stirred at room temperature for 3 hr. The mixture was filtered (weight of the solid, 3.64 g). Evaporation of the filtrate gave 16.69 g of a dark semi-solid which was stirred with ether (3 X 100 ml). The ether layers were separated and evaporated to give 10.60 g of the crude yellow product. It was recrystallized from methylcyclohexane, mp 98-100.

Anal. Calcd for C₆H₄N₂S₁F₃: C, 27.69; H, 1.54; N, 10.77.

Found: C, 28.16; H, 1.67; N, 10.70.

IR (Nujol): 3350, 1360, 1210, 1190, and 1140.

N,N'-bis(4-chloro-3-pyridyl)-N,N'-bis(trifluoromethylsulfonyl)oxamide

Oxalyl chloride (1.1 g; 0.0087 mole) diluted in 20 ml of THF was added dropwise to a solution of N-(4-chloro-3-pyridyl)trifluoromethanesulfonamide (3 g; 0.0145 mole) and triethylamine (1.6 g; 0.0016 mole) in 50 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature overnight. The white solid was separated (1.89 g) by filtration. Evaporation of the THF filtrate gave 4.05 g of a semi-solid, which solidified upon standing. It was recrystallized from methylcyclohexane, mp 95-98.

Anal. Calcd for C₁₄H₆N₂O₂S₂C₁₂F₆: C, 29.27; H, 1.05; N, 9.76.

Found: C, 28.87; H, 1.08, N, 9.71.

IR (CH₂C₁₂): 1730, 1450, 1420, 1350, 1260, 1210, and 1130.

3,5,6-Trichlorosalicylic acid, 2-(4-morpholinyl)ethyl ester (144)

To a solution of trichlorosalicylic acid (20 g; 0.0828 mole, recrystallized from toluene, mp 190-196 C) and N-2-hydroxyethylmorpholine (11.20 g; 0.0854 mole) in 220 ml of ethyl ether was added in portions a solution of DCC (17.26 g; 0.837 mole) in 75 ml of ethyl ether at room temperature under a nitrogen atmosphere. After the addition was complete, the mixture was stirred for 20 hr. The white solid precipitate (19.17 g; urea) was isolated by filtration. Evaporation of the ether filtrate gave 32.71 g of a yellow solid, which was purified by preparative HPLC (ethyl acetate as the eluent) to give the desired compound (14.97 g), mp 116-118.

Anal. Calcd for C₁₃H₁₄N₀O₄C₁₃: C, 44.01; H, 3.95; N, 3.95.

Found: C, 44.08, H, 3.94; N, 3.91.

IR (Nujol): 3400, 1730, 1420, 1360, 1270, 1220, and 1100.

NMR (acetone-d₆): 2.90 ppm, m, 4H; 3.05 ppm, t, 2H; 3.80 ppm, m, 4H; 4.70 ppm, t, 2H; 7.45 ppm, s, 1H; 9.05 ppm, s, 10H.

Attempted preparation of oxalic acid bis[3,5,6-trichloro-2-[(2-morpholinyl)ethoxy]carbonylphenyl] ester (146)

To a solution of 144 (3.54 g; 0.01 mole) and 4-dimethylaminopyridine (1.22 g; 0.01 mole) in 50 ml of dry THF was added dropwise a solution of oxalyl chloride (0.87 g; 0.069 mole) in 10 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was complete, the mixture was stirred at room temperature

for 3 hr. The white solid was filtered and washed with methylene chloride (weight of the solid, 3.12 g). The IR spectrum (3400, 2600, 1770, and 1730) of this solid suggested that it was the hydrochloride of the expected oxalate ester. However, attempts to purify this solid resulted in decomposition. The filtrate was evaporated to give 1.79 g of oil; its IR spectrum did not show a carbonyl band at 1770-1790 corresponding to the oxalate ester.

3,6,9,12,15-Pentaoxahexadecyl 3,5,6-trichlorosalicylate

To a solution of 10 g (0.049 mole) of trichlorosalicylic acid, 125 ml of ether, and 13.13 ml (0.49 mole) of 3,6,9,12,15-pentaoxahexadecanol at 0 C. and under nitrogen was added 11.02 g (0.053 mole) of N,N'-dicyclohexylcarbodiimide during 15 min. The above mixture was stirred at room temperature for 20 hr. The white solids (dicyclohexyl urea) were filtered off by vacuum filtration and discarded. The filtrate was stripped of solvent to yield 25.54 g of a white semi-solid. Cyclohexane (200 ml) was added to this semi-solid, and the mixture was stirred for 10 min. The bottom layer was stripped on a rotary evaporator to give 13.21 g of a light tarry oil. Purification of this oil by preparative HPLC gave a total of 6.39 g (29.6%) of a light oil.

IR (Neat): 3350, 1740, 1660, 1550, 1440, 1280, 1210, and 1100.

Bis[3,4,6-trichloro-2-[(3,6,9,12,15-pentaoxahexadecyl)oxy]carbonyl]-phenyl] oxalate (147)

To a solution of 3.29 g (0.0075 mole) of 3,6,9,12,15-pentaoxahexadecyl 3,5,6-trichlorosalicylate, 65 ml of THF, and 1.25 ml (0.0090 mole) of triethylamine at 0 C. under nitrogen, was slowly added 0.40 ml (0.0045 mole) of oxalyl chloride diluted in 20 ml of THF. The mixture was stirred at room temperature overnight. The triethylamine salt was filtered off and discarded. Evaporation of the filtrate on a rotary evaporator gave 4.82 g of a thick oil. Ether (20 ml) was added to the oil. The mixture was stirred for 10 min. The insolubles were filtered off, and solvent was removed from the filtrate on a rotary evaporator to give 2.96 g (65.5%) of a dark oil. Attempts to solidify or purify this oil by preparative HPLC were unsuccessful.

Anal. Calcd for C₃₈H₄₈O₁₈C₁₆: C, 45.37; H, 4.78.

Found: C, 45.08; H, 5.02.

IR (Nujol): 3500, 1800, 1780, 17490, 1280, and 1100.

3,6,9-Trioxadecyl 3,5,6-trichlorosalicylate

A solution of 10 g (0.049 mole) of trichlorosalicylic acid, 125 ml of ether, and 7.97 g (0.049 mole) of methoxytriglycol was cooled at 0 C. under nitrogen. N,N'-dicyclohexylcarbodiimide (11.02 g; 0.053 mole) was added during 15 min. The mixture was stirred at 0 C. for 1.5 hr and at room temperature for 2 hr. The white solids (dicyclohexyl urea) were filtered off by vacuum filtration and discarded. The filtrate was stripped on a rotary evaporator to give 13.6 g of a white semi-solid. The semi-solid was heated with acetonitrile, and the white solid precipitate was separated by vacuum filtration. The filtrate was stripped on a rotary evaporator to give

13.5 g of an oil which was purified by preparative HPLC (ethyl acetate).

Anal. Calcd for C₁₄H₁₇O₆C₁₃: C, 43.35; H, 4.39.

Found: C, 43.44; H, 4.53.

IR (Nujol): 3400, 1730, 1670, 1440, 1380, 1280, 1200, and 1110.

NMR (CDCl₃): 3.35 ppm, s, 3H; 3.65 ppm, m, 8H; 3.85 ppm, m, 2H; 7.55 ppm, s, 1H; 8.35 ppm, broad s, 1H (OH).

Bis[3,4,6-trichloro-2-[(3,6,9-trioxadecyl)oxy]carbonyl]phenyl oxalate (148)

A solution of 2.75 g (0.0078 mole) of 3,6,9-trioxadecyl 3,5,6-trichlorosalicylate, 50 ml of THF, and 1.31 ml (0.0094 mole) of triethylamine was cooled to 0 C. under nitrogen. Then 0.41 ml (0.0047 mole) of oxalyl chloride diluted in 20 ml of THF was slowly added. The mixture was stirred at room temperature for 4 hr. The triethylamine salt was isolated by vacuum filtration and discarded. The filtrate was stripped on a rotary evaporator to give 2.76 g of a dark oil. Purification of this oil by preparative HPLC (ethyl acetate as eluent) gave 1.16 g of a light yellow solid. Recrystallization of this solid from cyclohexane gave 0.45 g of a white solid, mp 60-62.

Anal. Calcd for C₂₈H₃₄O₁₄C₁₆: C, 41.63; H, 4.21.

Found: C, 41.91; H, 4.04.

IR (Nujol): 3400, 1740, 1720, 1440, 1370, 1270, 1230, and 1100.

4,8,12-Trioxatridecyl 3,5,6-trichlorosalicylate

A solution of 10.0 g (0.049 mole) of trichlorosalicylic acid, 125 ml of ether, and 10.0 g (0.049 mole) of tripropylene glycol methyl ether was cooled to 0 C. under nitrogen. Then 11.02 g (0.053 mole) of N,N'-dicyclohexylcarbodiimide (99%) was added over 15 min. The mixture was stirred at 0 C. for 30 min, then at room temperature for 3 hr. The white solid was filtered by vacuum filtration and discarded. The filtrate was stripped on a rotary evaporator to give 20.9 g of a white semi-solid which was stirred with 250 ml of acetonitrile for 45 min and filtered. Evaporation of the filtrate gave 15.74 g of a thin, light oil. Purification of this oil by preparative HPLC yielded a total of 8.14 g (45.0%) of an oil.

Anal. Calcd for C₁₇H₂₃O₆C₁₃: C, 47.50; H, 5.36.

Found: C, 46.38; H, 5.22.

IR (Nujol): 3400, 1740, 1680, 1560, 1420, 1370, 1280, 1250, 1200, and 1100.

Bis[3,4,6-trichloro-2-[(4,8,12-trioxatridecyl)oxy]carbonyl]-phenyl oxalate (150)

A solution of 7.0 g (0.0189 mole) of 4,8,12-trioxatridecyl 3,5,6-trichlorosalicylate, 130 ml of THF, and 3.17 ml (0.0227 mole) of triethylamine was cooled to 0 C. under nitrogen. Oxalyl chloride (0.99 ml; 0.0114 mole) diluted in 20 ml of THF was added slowly. The mixture was stirred at room temperature overnight. The triethylamine salt was isolated by vacuum filtration and discarded. Solvent was evaporated from the filtrate to give 6.69 g (64.3%) of an

oil.

Anal. Calcd for C₃₆H₄₄O₁₄C₁₆: C, 47.32; H, 4.82.

Found: C, 46.63; H, 5.05.

IR (Neat): 3450, 1800, 1750, 1420, 1370, 1260, and 1100.

3,6,9,12,15-Pentaoxahexadecyl 3,5-dichloro-4-hydroxybenzoate

To a suspension of 3,5-dichloro-5-hydroxybenzoic acid (20.7 g; 0.1 mole) and 3,6,9,12,15-pentaoxahexadecanol (26 g; 0.103 mole) in 150 ml of toluene was added 1 g of p-toluenesulfonic acid. The mixture was heated at reflux under a nitrogen atmosphere for 22 hr. A Dean-Stark condenser was attached to collect water from the reaction. The reaction mixture was cooled to room temperature, some white precipitate that had formed was separated by filtration, and the toluene filtrate was evaporated to give 49.30 g of oil. Purification by preparative HPLC (ethyl acetate) gave 32.9 g of the desired product as an oil.

IR (Neat): 3350, 1720, 1590, 1560, 1400, 1360, 1300, 1270 and 1120.

Bis[2,6-dichloro-4[(3,6,9,12,15-pentaoxahexadecyl)oxy]carbonyl]-phenyl] oxalate (151)

To a solution of 3,6,9,12,15-pentaoxahexadecyl 3,5-dichloro-4-hydroxybenzoate (4.41 g; 0.01 mole) and triethylamine (1.2 g; 0.012 mole) in 40 ml of dry THF was added dropwise a solution of oxalyl chloride (0.8 g; 0.0063 mole) in 10 ml of THF at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for 4 hr. The white solid was filtered (1.65 g), and evaporation of the filtrate gave 4.85 g of the desired product as an oil. Attempts to purify the product by preparative HPLC were unsuccessful.

4-Hydroxy-2,3,5-trichlorobenzenesulfonyl chloride (152) and 4-hydroxy-2,3,5-trichlorobenzenesulfonic acid

To 84.15 ml (1.266 mole) of chlorosulfonic acid, cooled to 0 C. under nitrogen, was slowly added 49.99 g (0.253 mole) of 2,4,6-trichlorophenol. The mixture thickened after the addition; another 28 ml of chlorosulfonic acid was added slowly. The mixture was heated to 95 C. in an oil bath for 3 hr, cooled to room temperature, and allowed to stir overnight. The mixture was drowned into 1.5 liters of ice water. The gummy residue which formed was dissolved in 800 ml of methylene chloride and dried over sodium sulfate. The methylene chloride was stripped on a rotary evaporator to give 51.64 g of 152 as a light tan solid.

IR (Nujol): 3400, 1550, 1360, 1170, and 1130.

To 51.64 g of 152 was added 725 ml of water, and the mixture was heated on a steam bath at 85-90 C. for 30 min. The mixture was filtered, and the aqueous portion was stripped on a rotary evaporator to give 38.65 g of 4-hydroxy-2,3,5-trichlorobenzenesulfonic acid as a white solid, mp 145-147.

IR (Nujol): 3400, 1560, 1440, 1370, 1300, 1200, 1160, and 1130.

NMR (DMSO-d₆): 7.8 ppm, s, 1H; 8.35 ppm, s, 4H.

Tetramethylammonium salt of 4-hydroxy-2,3,5-trichlorobenesulfonic acid (153)

To 20 g (0.068 mole) of 4-hydroxy-2,3,5-trichlorobenesulfonic acid was added 300 ml of water, and the solution was stirred (pH 1-2). To the solution was added slowly with stirring 35.05 ml of tetramethylammonium hydroxide (20% in methanol solution). During the addition a white precipitate formed. The final pH was 4-5.

The aqueous suspension was stripped on a rotary evaporator to give 48.90 g of a white solid, which was recrystallized from acetonitrile to yield 16.12 g of white crystals, mp 242-243.

Anal. Calcd for C₁₀H₁₄N₀4S C₁₃: C, 34.27; H, 3.99; N, 3.99; S, 9.15.

Found: C, 32.77; H, 4.32; N, 4.07; S, 9.41.

IR (Nujol): 3400, 1650, 1540, 1480, 1370, 1300, 1240, and 1180.

NMR (DMSO-d₆): 3.2 ppm, s, 12H; 7.9 ppm, s, 1H; 10.0 ppm, s, 1H (OH).

Bis(tetramethylammonium) salt of 4,4'-(oxalyldioxy)-bis(2,3,5-trichlorobenesulfonic acid) (7,STPCO)

A solution of 6.0 g (0.017 mole) of 153, 90 ml of dry methylene chloride, and 1.74 g (0.017 mole) of triethylamine was cooled to 0°C. under nitrogen, and 0.86 ml of oxalyl chloride diluted in 10 ml of methylene chloride was added during 35 min. The solution was allowed to stir at room temperature overnight. The white solids were isolated by vacuum filtration and washed with methylene chloride and then with ether to give 5.79 g of the crude product. It was recrystallized from acetonitrile, mp 229-231.

Anal. Calcd for C₂₂H₂₆O₁₀N₂C₁₆S₂: C, 34.99; H, 3.44; N, 3.71; Cl 28.17; S, 8.49.

Found: C, 34.42; H, 3.06; N, 3.71; Cl, 27.61, S, 7.79.

IR (Nujol): 3400, 1780, 1540, 1490, 1370, 1290, 1220 and 1180.

NMR (DMSO-d₆): 3.20 ppm, s, 12H; 7.80 ppm, s 1H.

4,4'-(Oxalyldioxy)-bis(2,3,5-trichlorobenesulfonic acid, bis(tetraethyl)ammonium salt (154)

To 10 g (0.039 mole) of 4-hydroxy-2,3,5-trichlorobenesulfonic acid was added 150 ml of water (pH of the solution, 1-2). A solution of tetraethylammonium hydroxide (20% in water) was slowly added with stirring until the pH of the solution was about 5. The solution was further stirred for 30 min and filtered. Evaporation of the solution gave 13.6 g of solid which was further treated with THF. The THF solution was filtered and evaporated to give 12.60 g of the tetraethylammonium salt of 4-hydroxy-3,5,6-trichlorobenesulfonic acid, mp 160-162.

Anal. Calcd for C₁₄H₂₂N₀4C₁₃S: C, 41.33; H, 5.41; N, 3.44.
Found: C, 41.74; H, 5.82; N, 3.78.

To the above salt (4 g; 0.01 mole) and 3A molecular sieves (8 g) suspended in 60 ml of dry methylene chloride was added dropwise a solution of oxalyl chloride (0.73 g; 0.0057 mole) in 20 ml of methylene chloride at room temperature under a nitrogen atmosphere.

After the addition was completed the mixture was heated at reflux overnight. The mixture was filtered, and the filtrate was evaporated to give 4.2 g of the crude hygroscopic white solid product (138). It was recrystallized from acetonitrile-ether, mp 118-121.
IR (CH₂C₁₂): 3450, 1800, 1780, 1620, 1480, 1410, 1350, 1260, 1220, and 1100.

4,4'-(Oxalyldioxy)-bis(2,3,5-trichlorobenzenesulfonic acid, bis(tetrabutyl)ammonium salt (155)

To 15 g (0.0585 mole) of 4-hydroxy-2,3,5-trichlorobenzenesulfonic acid was added 225 ml of water (pH of the solution, 1-2). To this mixture was slowly added 33.15 ml of tetrabutylammonium hydroxide (40% in water). The resulting mixture was stirred at room temperature for 30 min. The white solid was isolated by filtration and dried in vacuum to give 19.15 g of the tetrabutylammonium salt of 4-hydroxy-3,5,6-trichlorobenzenesulfonic acid, mp 144-145.
Anal. Calcd for C₂₂H₃₈N₁₀C₁₃S: C, 50.92; H, 7.33; N, 2.70. Found: C, 51.03; H, 7.17; N, 2.80.

Oxalyl chloride (1.455 g; 0.0115 mole) in 5 ml of methylene chloride was added dropwise to a suspension of the tetrabutylammonium salt of 4-hydroxy-3,5,6-trichlorobenzenesulfonic acid (10 g; 0.0193 mole) and 3A molecular sieves (20 g). After the addition, the mixture was heated at reflux overnight under nitrogen. The solution was filtered; evaporation of the filtrate gave 10.55 g of the desired product, 139, as a gummy solid.
IR (CH₂C₁₂): 3450, 1800, 1780, 1560, 1460, 1420, 1360, 1260, 1230, and 1100.

4,4'-(Oxalyldioxy)-bis(3-chloro)benzenesulfonic acid, bis(tetramethyl)ammonium salt (159)

A solution of 5.88 g (0.021 mole) of the tetramethylammonium salt of 4-hydroxy-3-chlorobenzenesulfonic acid (prepared according to the procedure for 153), 125 ml of methylene chloride, and 2.90 ml (0.031 mole) of triethylamine was cooled to 0 C. under nitrogen. Oxalyl chloride (1.05 ml, 0.01 mole) diluted with 20 ml of methylene chloride was slowly added. The solution was allowed to stir at room temperature for 4 hr. A white solid was isolated by vacuum filtration; the solid was washed with methylene chloride, then with ether. The solid was slurried in 100 ml of methylene chloride for 10 min, then filtered and washed with methylene chloride and then with ether to give 5.9 g of crude product. The crude product was recrystallized from acetonitrile, mp >260.
Anal. Calcd for C₂₂H₃₀O₁₀N₂C₁₂S₂: C, 42.80; H, 4.86; N, 4.53. Found: C, 42.38; H, 5.00; N, 4.75.
IR (Nujol): 3400, 1760, 1370, 1200, 1140, and 1100.
NMR (DMSO-d₆): 3.20 ppm, s, 12H; 7.7 ppm, m, 3H.

4,6-Dichloro-3-dimethylaminophenol hydrochloride

A solution of 3-dimethylaminophenol (30 g; 0.219 mole) in 200 ml of methylene chloride was cooled to 0 C. under a nitrogen atmosphere. Sulfuryl chloride (118.07 g; 0.975 mole) was added very slowly during 1.5 hr. After the addition was completed, the mixture was heated gently on a steam bath for 4 hr. The solid was collected by vacuum filtration and washed with methylene chloride (wt, 3.77 g). Recrystallization from acetonitrile - 3A alcohol (100 ml-40 ml) gave pure 4,6-dichloro-3-dimethylaminophenol hydrochloride, mp 209-213.
Anal. Calcd for C₈H₁₀N₁OCl₃: C, 39.59; H, 4.12; N, 5.77.
Found: C, 39.47; H, 4.02; N, 5.99.
NMR (DMSO-d₆): 2.9 ppm, s, 6H; 7.3 ppm, s, 1H; 11 ppm, s, 2H.

Evaporation of the filtrate gave 62.77 g of a semi-solid which was identified as 2,4,6-trichloro-3-dimethylaminophenol hydrochloride (see below).

Bis(2,4-dichloro-3-dimethylaminophenyl) oxalate (164)

A solution of 4,6-dichloro-3-dimethylaminophenol hydrochloride (3.23 g; 0.013 mole) and triethylamine (2.7 g; 0.027 mole) in 100 ml of methylene chloride was cooled to 0 C. under a nitrogen atmosphere. Oxalyl chloride (1.01 g; 0.008 mole) diluted in 5 ml of methylene chloride was added dropwise with stirring. After the addition was completed the mixture was stirred at room temperature overnight. Evaporation of the solvent on a rotary evaporator gave 6.57 g of an oil which was treated with THF. The white solid thus formed was filtered, and evaporation of the THF filtrate gave 3.22 g of oil. The IR spectrum of this oil had a C=O absorption at 1760, indicating the expected oxalate ester. Attempts to solidify this oil were unsuccessful.

[Oxalyl-bis[oxy(4,6-dichloro-3-phenylene)]bis(trimethylammonium-trifluoromethanesulfonamide) (166)

To a solution of 164 (2.4 g; 0.004 mole) in 30 ml of methylene chloride was added 2 ml of methyl trifluoromethanesulfonate. The mixture was stirred at room temperature for 2 hr. The white solid was isolated by filtration, washed with methylene chloride, and dried (wt, 1.46 g), mp 236-240.
Anal. Calcd for C₂₂H₂₂N₂O₁₀F₆: C, 33.25; H, 2.77; N, 3.53.
Found: C, 33.41; H, 2.39; N, 3.30.
IR (Nujol): 3450, 1780, 1370, 1240, 1220, and 1150.

2,4,6-Trichloro-3-dimethylaminophenol hydrochloride (161)

A solution of 100 g (0.729 mole) of 3-dimethylaminophenol and 500 ml of dry methylene chloride was cooled to 0 C. under nitrogen. Sulfuryl chloride (393.5 g; 2.916 mole) was added very slowly with stirring during 1.75 hr. The reaction mixture was refluxed on a steam bath for 22 hr. The white solid which formed was collected by vacuum filtration and washed with methylene chloride. The yield of product was 80.08 g (19.83%), mp 146-150.
Anal. Calcd for C₈H₉N₁OCl₃: C, 34.69; H, 3.28; N, 5.06.
Found: C, 34.50; H, 3.48; N, 4.60.
NMR (DMSO-d₆): 2.7 ppm, s, 6H; 7.4 ppm, s, 1H (exchanged with D₂O);

11.1 ppm, s, 1H (exchanged with D₂O).

Bis(2,4,6-trichloro-3-dimethylaminophenyl) oxalate (162)

A solution of 30 g (0.108 mole) of 2,4,6-trichloro-3-dimethylaminophenol hydrochloride, 400 ml of dry methylene chloride, and 24.11 g (0.238 mole) of triethylamine was cooled to 0 C. under nitrogen. Oxalyl chloride (8.25 g; 0.065 mole) diluted with 15 ml methylene chloride was added during 40 min with stirring. The solution was stirred overnight at room temperature. A white solid (18.72 g), triethylamine hydrochloride, was filtered and washed with methylene chloride. The filtrate was stripped on a rotary evaporator to give 44.11 g of a greyish-yellow solid. Tetrahydrofuran (300 ml) was added, and the mixture was stirred. Additional triethylamine hydrochloride (10.39 g) precipitated and was filtered off. The filtrate was stripped on a rotary evaporator to give 28.94 g of a beige solid. Recrystallization of this solid from 120 ml of acetonitrile gave 18.89 g (32.82%) of a beige-white solid, mp 116-118.

Anal. Calcd for C₃₆H₁₄O₄C₁₆N₂: C, 40.41; H, 2.65; N, 5.24.

Found: C, 40.40; H, 2.18; N, 5.33.

IR (Nujol): 1780, 1420, 1370, and 1100.

NMR (CDCl₃): 3.00 ppm, s, 12H; 7.5 ppm, s, 2H.

3,5-dimorpholinophenol

Following a literature procedure, dry phloroglucinol (63 g; 0.5 mole) and morpholine (87 ml; 1.0 mole) were condensed by heating for 24 hr at 200-220 C. in an autoclave, no external pressure being added. Recrystallization from n-butyl acetate yielded the desired compound (60 g; 45%), mp 164-167.

Anal. Calcd for C₁₄H₂₀N₂O₃: C, 63.64; H, 7.58; N, 10.61.

Found: C, 63.26; H, 7.49; N, 10.10.

IR (Nujol): 3250, 1580, 1260, 1180, 1160, 1100, and 995.

NMR (CDCl₃/DMSO-d₆): 2.9-3.3 ppm, m, 4H.

Mass spectrum (EI): m/e 265.

Bis-3,5-dimorpholinophenyl oxalate (168)

To a stirred, ice-cooled solution of 3,5-dimorpholinophenol (10.6 g; 0.04 mole) in 150 ml of THF under a nitrogen atmosphere was added, dropwise during 25 min, triethylamine (5.6 ml; 0.04 mole) diluted with 15 ml of THF. Oxalyl chloride (1.7 ml; 0.02 mole) diluted in 10 ml THF was added dropwise during 15 min, causing a white precipitate. The resulting suspension was stirred at room temperature for 24 hr. The filtered solid was found to be a mixture of triethylamine hydrochloride and product. Separation was achieved by stirring the solid in cold water for 15 min, filtering, and washing the filter cake with cold water, cold 2-propanol, and finally with hexane. The solid was dried under vacuum, then dissolved in ethylene dichloride, which was then removed under reduced pressure, leaving a light yellow solid (5.9g; 50%).

Anal. Calcd for C₃₀H₃₈N₄O₈: C, 61.85; H, 6.53; N, 9.62.

Found: C, 59.66; H, 6.45; N, 9.06.

IR (Nujol) 1760, 1600, 1580, 1260, 1180, 1120, 1009, 999, and 875.

4,4'-[*(1,2-Dioxo-1,2-ethanediyl)bis(oxy-1,3,5-benzenethyl)*] tetrakis-(4-methylmorpholinium trifluoromethanesulfonate) (169)

To an ice-cooled stirred suspension of 168 (1.45 g; 0.0025 mole) in 125 ml of methylene chloride was added, during 30 min, methyl triflate (1.13 ml; 0.10 mole) diluted with 20 ml of methylene chloride. The suspension was allowed to reach room temperature and held there for 60 hr. A white solid was obtained by filtration, washed with methylene chloride, and dried under vacuum (1.7 g; 55%).

2,6-Dichloro-4-(morpholinomethyl)phenol

Morpholine (19.2 ml; 0.22 mole) was added dropwise during 20 min to a stirred solution of 2,6-dichlorophenol (32.6 g; 0.20 mole) dissolved in 400 ml of 50% aqueous ethanol. A solution of 37% formalin (16.4 ml; 0.22 mole) dissolved in 25 ml of water was added dropwise during 15 min. The resulting solution was refluxed under a nitrogen atmosphere for 20 hr. The dark red solution was evaporated under reduced pressure to give a pink semi-solid, which was redissolved in a 50:50 mixture of ethanol:toluene. Evaporation under reduced pressure yielded a pink solid, which was recrystallized, following treatment with activated charcoal, from 2-propanol, (35.3 g; 78%), mp 132-135.
 IR (Nujol): 3300, 1480, 1415, 1350, 1280, 1140, 1105, 875, and 790.
 NMR (CDCl₃): 7.2 ppm, s, 2H (aromatic); 8.63 ppm, s, 1H (exchanged with D₂O, OH); 3.5-3.8 ppm, m, 4H (next to morpholine O); 3.3 ppm, s, 2H (benzylic); 2.2-2.5 ppm, m, 4H (next to morpholine N).

Bis[2,6-dichloro-4-[(4-morpholinyl)methyl]phenyl] oxalate 170)

Under a nitrogen purge, triethylamine (7.7 ml; 0.055 mole) diluted with 15 ml of THF was added dropwise during 20 min to an ice-cooled solution of 2,6-dichloro-4-(morpholinomethyl)phenol (13.0 g; 0.05 mole) in 200 ml of THF. To this solution was added dropwise during 25 min a solution of oxalyl chloride (2.2 ml; 0.025 mole) diluted with 15 ml of THF, causing the formation of a white precipitate. The suspension was stirred for 2.5 hr at room temperature, after which time an NMR spectrum of a small aliquot showed about an 80% conversion. The solution was cooled once more to ice temperature, and additional triethylamine (2.2 ml; 0.016 mole) and oxalyl chloride (0.8 ml; 0.016 mole) were added dropwise sequentially. Stirring for a further 2.5 hr completed the conversion to the desired oxalate ester. Triethylamine hydrochloride was removed by filtration, and the filter cake was washed with THF (2 X 50 ml). Removal of THF under reduced pressure yielded a yellow solid. Recrystallization from ethyl acetate yielded a white solid (5.3 g; 37%) which was collected by filtration, mp 122-126.
Anal. Calcd for C₂₄H₂₄C₁₄N₂O₆: C, 49.83; H, 4.15; N, 4.84.
 Found: C, 50.05; H, 4.84; N, 5.15.
 IR (Nujol): 1760, 1560, 1235, 1105, 1005, 900, 875, and 860.

4,4'-(1,2-Dioxo-1,2-ethanediyl)bis[oxy(2,6-dichloro-4,1-phenylene)-methylene] bis(4-methylmorpholinium trifluoromethanesulfonate) (173)

Under a nitrogen atmosphere, 170 (0.5 g; 0.0012 mole) was suspended in 100 ml of ice-cold methylene chloride. Methyl triflate (0.26 ml; 0.0023 mole) diluted in 10 ml of methylene chloride, was added dropwise during 20 min. The suspension was stirred for 20 hr at room temperature. Filtration yielded a white solid which was washed with methylene chloride (2 X 25 ml) and hexane (25 ml) and dried under vacuum (0.80 g; 92%).

4-(Morpholino)methyl-2,3,6-trichlorophenol

Under a nitrogen purge, a solution of morpholine (9.5 ml; 0.11 mole) diluted with 25 ml of water was added dropwise during 20 min to a stirred solution of 2,3,6-trichlorophenol (19.7 g; 0.10 mole) dissolved in 200 ml of 50% aqueous ethanol. During the subsequent dropwise addition of 37% formalin (8.2 ml; 10.11 mole) diluted with 25 ml of water, a precipitate formed. Heating the solution to reflux caused the solid to dissolve; after 30 min precipitation occurred again. The solution was refluxed for an additional 2.5 hr, cooled, and a white solid removed by filtration. The filtrate was evaporated to dryness on a rotary evaporator, yielding a pink solid which was recrystallized, following treatment with activated charcoal, from hot 2-propanol to give a white solid. The melting point of both solids was 146-150.

Anal. Calcd for C₁₁H₁₂C₁₃N₀2: C, 44.52; H, 4.05; N, 4.72; Cl, 34.25.

Found: C, 44.73; H, 4.12; N, 4.65; Cl, 34.25.

IR (Nujol) 3600, 1540, 1395, 1280, 1260, 1160, 1110, 1085, 1000, 980, 920, 910, 865, 805, and 790.

Bis[2,3,5-trichloro-4-[(4-morpholiny)ethyl]phenyl] oxalate (171)

Under a nitrogen atmosphere, triethylamine (4.2 ml; 0.03 mole) diluted in 15 ml of THF was added dropwise during 25 min to a stirred, ice-cooled solution of 4-(morpholino)methyl-2,3,6-trichlorophenol in 175 ml of THF. Oxalyil chloride (1.3 ml; 0.015 mole) diluted with 20 ml of THF was added dropwise during one hr. The reaction mixture was stirred at room temperature for 45 min, and the triethylamine salt was removed by filtration. Evaporation of solvent under reduced pressure yielded a gummy, white solid (9.6 g; quantitative). Recrystallization from methycyclohexane yielded a white, powdery solid, mp 110-114.

Anal. Calcd for C₂₄H₂₂C₁₆N₂O₆: C, 44.51; H, 3.40; N, 4.32.

Found: C, 45.83; H, 3.75; N, 4.85.

IR (Nujol): 1780, 1300, 1105, 870, 790, and 725.

4,4'-(1,2-Dioxo-1,2-ethanediyl)bis[oxy(2,3,5-trichloro-4,1-phenylene)-methylene] bis(4-methylmorpholinium trifluoromethanesulfonate) (174)

Under a nitrogen atmosphere 171 (3.2 g; 0.005 mole) was suspended in 125 ml of cold methylene chloride. During 40 min, methyl triflate (1.1 ml; 0.01 mole) diluted in 20 ml of methylene chloride was added dropwise, causing most of the solid to dissolve.

The solution was allowed to warm to room temperature and then stirred for 20 hr, resulting in a white suspension. The solid was collected by filtration, washed with methylene chloride (2 X 25 ml), and dried under vacuum (4.6 g; 96%).

4-(Morpholinomethyl)-2,3,5,6-tetrachlorophenol

Under a nitrogen purge morpholine (9.6 ml; 0.11 mole) diluted in 25 ml of ethanol was added dropwise during 20 min to a stirred solution of 2,3,4,6-tetrachlorophenol (23.2 g; 0.1 mole) dissolved in 200 ml of 30% aqueous ethanol. A white precipitate resulted upon the dropwise addition of 37% formalin (8.2 ml; 0.11 mole) dissolved in 25 ml of ethanol. The suspension was stirred for one hr at room temperature and 3.5 hr at reflux. The mixture was cooled to ice temperature, and the white precipitate was collected by filtration. The solid was recrystallized from THF to give a white powder, mp 192-196, dec. (21 g; 56%).

Anal. Calcd for C₁₁H₁₁C₁₄N₀2: C, 39.88; H, 3.32; N, 4.23; Cl, 42.90.

Found: C, 40.31; H, 3.41; N, 4.29; Cl, 41.49.

IR (Nujol): 3350, 1480, 1410, 1280, 1140, 1105, 875, and 790.

Bis[2,3,5,6-tetrachloro-4-[(4-morpholinyl)methyl]phenyl] oxalate (172)

Under a nitrogen atmosphere, triethylamine (3.0 ml; 0.022 mole) diluted in 15 ml of THF, was added dropwise during 30 min to a stirred, ice-cooled suspension of 4-(morpholinomethyl)-2,3,5,6-tetrachlorophenol (6.6 g; 0.02 mole) in 125 ml of THF, during which time the solid all dissolved. Oxalyl chloride (0.87 ml; 0.01 mole) diluted in 1 ml of THF was added dropwise during 30 min, causing the formation of a white precipitate. The suspension was stirred at room temperature for 2.5 hr and filtered. The resulting solid was found to be a mixture of triethylamine hydrochloride and product. The solid was stirred in 150 ml of methylene chloride to remove the salt, filtered, washed with methylene chloride (2 X 25 ml), and dried under vacuum (4.3 g; 66%). Recrystallization from ethyl acetate afforded the product as shiny white crystals, mp 200-203.

IR (Nujol): 1780, 1350, 1270, 1250, 1125, 1100, 995, 855, and 705.

Bis(2-chloro-3-pyridyl)oxalate (40)

To a solution of 3-hydroxy-2-chloropyridine (12.95 g; 0.1 mole) and triethylamine (11 g; 0.11 mole) in dry THF (120 ml) was added dropwise 6 ml (0.069 mole) of oxalyl chloride at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for 2 hr. Evaporation of the solvent gave a tan solid product which was treated with methylene chloride (200 ml). The white precipitate (17.98 g) was separated by filtration followed by stirring with 100 ml of water. The white solid that remained was collected by filtration and dried under vacuum (9.7 g), mp 175-178.

Anal. Calcd for C₁₂H₆N₂O₄C₁₂: C, 46.01; H, 1.92; N, 8.95.
Found: C, 46.70; H, 2.04; N, 8.92.

The original methylene chloride solution was also evaporated to dryness and treated with water (100 ml) to give an additional 5 grams of the product.

2-Chloro-3-hydroxy-1-methyl-pyridinium-trifluoromethanesulfonate oxalate (2:1) (177)

To a suspension of 40 (3.13 g; 0.01 mole) in methylene chloride (30 ml) was added 3 ml (0.0265 mole) of methyl trifluoromethanesulfonate at room temperature. The mixture was stirred for 4 hr. The white solid product was collected by filtration and washed with methylene chloride (wt, 3.5 g), mp 155-160.

Anal. Calcd for C₁₆H₁₂N₂O₁₀F₆C₁₂S₂: C, 29.95; H, 1.87; N, 4.37. Found: C, 29.12; H, 1.53; N, 4.29.

5-Chloro-8-quinolinol Oxalate (2:1)

To a solution of 5-chloro-8-hydroxyquinoline (10 g; 0.056 mole) in 5.63 g (0.056 mole) of triethylamine and 100 ml of dry THF, was added dropwise 2.79 ml (0.028 mole) of oxalyl chloride at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for an additional 2 hr. The insoluble solid was isolated by filtration. Evaporation of the filtrate gave 8.65 g of the product, mp 150-155.

Anal. Calcd for C₂₀H₁₀N₂O₄C₁₂: C, 58.11; H, 2.42; N, 6.78. Found: C, 57.85; H, 2.51; N, 6.63.

5-Chloro-8-hydroxy-1-methyl-quinolinium methanesulfate oxalate (2:1)(179)

Eighteen grams (0.1 mole) of 5-chloro-8-hydroxyquinoline and 100 ml of dimethyl sulfate were heated at 100 C. for 30 min. The mixture was cooled to room temperature, and the solid was collected by filtration and recrystallized from ethanol to give 5-chloro-8-hydroxy-1-methyl quinolinium methanesulfate (22.32 g), mp 198-200.

Anal. Calcd for C₁₁H₁₂N₀5ClS: C, 43.21; H, 3.96; N, 4.58; S, 10.49.

Found: C, 43.35; H, 3.98; N, 4.53; S, 10.64.

To a suspension of this quaternized hydroxyquinoline (15.5 g; 0.05 mole) in 5.13 g of triethylamine and 100 ml of methylene chloride was added dropwise 2.5 ml (0.025 mole) of oxalyl chloride at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for an additional 4 hr. The yellow solid was collected by filtration, washed with methylene chloride, and dried. The pure compound was obtained by further washing with nitromethane (wt, 6.78 g), mp 178-180.

5,7-Dichloro-8-quinolinol Oxalate (2:1) (43)

To a suspension of 21.4 g (0.1 mole) of 5,7-dichloro-8-hydroxyquinoline in 11 g of triethylamine (0.11 mole) and 25 ml of dry THF was added dropwise 5 ml (0.05 mole) of oxalyl

chloride at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for an additional 3 hr. The white precipitate was separated by filtration and dried in vacuum at 60 C. to give 18 g of the product, mp 203-206.

Anal. Calcd for C₂₀H₁₈N₂O₄C₁₄: C, 49.79; H, 1.66; N, 5.81.
Found: C, 49.12; H, 1.83; N, 5.68.

5,7-Dichloro-8-hydroxy-1-methylquinolinium methanesulfonate oxalate (2:1) (180)

Twenty grams (0.093 mole) of 5,7-dichloro-8-hydroxyquinoline and 100 ml of dimethyl sulfate were heated at 100 C. for 3 hr. The mixture was cooled to room temperature, and the solid was collected by filtration (wt, 19.37 g). Recrystallization of the product from nitromethane gave 14.1 g of 5,7-dichloro-8-hydroxy-1-methyl quinolinium methanesulfate, mp 200-204.

Anal. Calcd for C₁₁H₁₁N₀S₀C₁₂: C, 38.83; H, 3.24; N, 4.12.
Found: C, 38.57; H, 3.23; N, 4.72.

To a suspension of this quaternized hydroxyquinoline (7.0 g; 0.02 mole) in 2.09 g of triethylamine and 100 ml of methylene chloride was added dropwise 1.1 ml (0.011 mole) of oxalyl chloride at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature for additional 2 hr. The product was collected by filtration and washed with methylene chloride to give 6.33 g of product, mp 155-160.

Anal. Calcd for C₂₄H₂₀N₂O₁₂S₂C₁₄: C, 39.24; H, 2.72; N, 3.81.
Found: C, 38.85; H, 2.81; N, 3.95.

4-Hydroxy-7-(trifluoromethyl)-3-quinoline carboxylic acid ethyl ester oxalate (2:1)

To a solution of ethyl 4-hydroxy-7-trifluoromethyl-3-quinoline carboxylate (15 g; 0.053 mole) in triethylamine (5.5 g; 0.055 mole) and methylene chloride (100 ml) was added dropwise 2.5 ml (0.0287 mole) of oxalyl chloride at 0 C. under a nitrogen atmosphere. After the addition was completed the mixture was stirred at room temperature. Product was isolated by filtration, washed with methylene chloride, and dried (wt, 7.5 g), mp 270.

Anal. Calcd for C₂₈H₁₈N₂O₈F₆: C, 53.85; H, 2.88; N, 4.49.
Found: C, 53.38, H, 3.28; N, 4.51.

4-Hydroxy-3-carboxy-1-methyl-7-(trifluoromethyl)quinolinium trifluoromethanesulfonate ethyl ester oxalate (2:1) (181)

To a suspension of 2.0 g (0.0032 mole) of 4-hydroxy-7-trifluoromethyl-3-quinoline carboxylic acid ethyl ester oxalate (2:1) in 50 ml of methylene chloride was added 2 ml (0.0177 mole) of methyl trifluoromethanesulfonate. The mixture was stirred at room temperature for 20 hr. The solid product was collected by filtration, washed with methylene chloride, and dried (wt, 1 g), mp 160-164.

N,N,N',N'-tetra-4-pyridinylethanediamide (182)

Following a literature procedure, 4-aminopyridine (31 g; 0.33 mole), phosphorous trichloride (29 ml; 0.32 mole) and pyridine (60 ml; 0.74 mole) were reacted to form 4,4'-dipyridylamine. Recrystallization from water gave white needles of mp 274-279 (lit. mp 273-277.).

Anal. Calcd for C₁₀H₉N₃: C, 70.18; H, 5.26; N, 24.56.

Found: C, 69.67; H, 5.45; N, 24.53.

IR (Nujol): 1580, 1340, 1205, 1000, 990, and 810.

NMR (DMSO-d₆): 7-9 ppm, m, 8H (aromatic), 3.5 ppm, s, 1H (NH, exchanged with D₂O).

Under a nitrogen atmosphere, triethylamine (5.6 ml; 0.04 mole) diluted in 15 ml of THF was added dropwise during 20 min to an ice-cooled, stirred suspension of 4,4'-dipyridylamine (6.8 g; 0.04 mole) in 200 ml of THF. Dropwise addition of oxalyl chloride (1.8 ml; 0.02 mole), diluted in 15 ml of THF, caused considerable misting, so the addition rate was kept very slow. The suspension was stirred 56 hr at room temperature, filtration leaving a white filter cake of product and triethylamine hydrochloride salt. The solid was extracted with 400 ml of boiling THF, removing the salt by filtration. The white solid that precipitated from the chilled filtrate was recrystallized from hot THF, mp 247-251.

Anal. Calcd for C₂₂H₁₆N₆O₂: C, 66.67; H, 4.04; N, 21.21.

Found: C, 65.13; H, 4.58; N, 20.45.

IR (Nujol): 1680, 1570, 1485, 1360, 1270, 1210, 1195, 995, and 825.

4,4'-[(1,2-dioxo-1,2-ethanediyl)bis(nitrilo)] tetrakis(1-methyl-pyridinium trifluoromethanesulfonate) (183)

Under a nitrogen purge, methyl trifluoromethanesulfonate (4.5 ml; 0.04 mole) diluted with 20 ml of methylene chloride was added dropwise during 30 min to a stirred, ice-cooled suspension of finely-ground bis (4,4'-dipyridyl) oxamide (3.64 g; 0.01 mole) in 80 ml of methylene chloride. After being held at ice temperature for 2 hr, the suspension was stirred at room temperature for 24 hr. The white solid obtained by filtration was washed with methylene chloride (2 X 25 ml), and hexane (2 X 25 ml), and air-dried under vacuum, mp 114-122.

Anal. Calcd for C₃₀H₂₈F₁₂N₆O₁₄S₄: C, 34.22; H, 2.66; F, 21.67; N, 7.98; S, 12.17.

Found: C, 33.43; H, 2.85; F, 21.65; N, 8.17; S, 13.27.

IR (Nujol): 2950, 1710, 1620, 1500, 1360, 1220, 1140-1080 (broad), 1025, 910, and 840.

2,3-dihydro-2-oxo-benzoxazole-6-sulfonylchloride (185)

Following a literature procedure, 2-benzoxazolinone (33.8 g; 0.25 mole) and chlorosulfonic acid (85 ml; 1.25 mole) were condensed. Recrystallization of the precipitated solid from 5:1 toluene/acetonitrile yielded the product as shiny, beige crystals (11.5 g; 20%), mp 178-184.

Anal. Calcd for C₇H₄ClN₄O₄S: C, 35.97; H, 1.71; Cl, 15.20;

N, 6.00; S, 13.70.

Found: C, 35.55; H, 1.93; Cl, 11.98; N, 4.47; S, 12.49.

IR (Nujol): 3100, 1890, 1770, 1610, 1410, 1300, 1270, 1240, 1180, 1050, 950, 890, 870, 820, 760, and 710.

NMR (CDCl₃): 7.2-8.0 ppm, m, 3H (aromatic); 3.2 ppm, s, 1H (NH, D₂O exchanged).

2,3-dihydro-2-oxo-benzoxazole-6-sulfonic acid, tetramethylammonium salt (186)

A suspension of 185 (5.8 g; 0.025 mole) in 150 ml water was refluxed for 2.5 hr, during which time all the solid dissolved. Water was evaporated under high vacuum, leaving an amber semi-solid, (5.3 g; theoretical).

The entire solid was dissolved in water and 20% tetramethylammonium hydroxide in methanol (13 ml; 0.025 mole) was added dropwise until the solution was neutral to pH paper. The solution was evaporated under reduced pressure, fresh methanol was added, and the solution was concentrated again. Addition of ether caused the immediate precipitation of a beige, solid which was collected by filtration and air-dried. The material recrystallized, after Darco treatment, from 2:1 ethanol/2-propanol as off-white crystals (6.3 g). Even after prolonged treatment in a vacuum apparatus, the salt retained a mole of water of crystallization, mp 134-140.

IR (Nujol): 3390, 1795, 1700, 1560, 1270, 1240, 1210, 1140, 1065, 1020, 940, and 920.

NMR (DMSO-d₆): 6.8-7.5 ppm, m, 3H (aromatic), 5.3 ppm, broad s, 2H (NH), 3.1 ppm, s, 16H (N(CH₃)₄ + 2H₂O).

3,3'-(1,2-Dioxo-1,2-ethandiyl)bis(2,3-dihydro-2-oxo-6-benzoxazole-sulfonic acid), bis(tetramethylammonium salt) (187)

A suspension of finely ground 186 (3.06 g; 0.01 mole) in 100 ml of dry acetonitrile was chilled in an ice bath. Under a nitrogen purge, triethylamine (4.2 ml; 0.03 mole) diluted in 10 ml of dry acetonitrile was added during 15 min to the stirred mixture. Oxalyl chloride (1.3 ml; 0.015 mole) diluted with 10 ml of dry acetonitrile was added during 25 min to the suspension, which was stirred for 1 hr at ice temperature and 60 hr at room temperature. The suspension was filtered, yielding a white solid which was stirred for 45 min with 200 ml of methylene chloride to remove triethylamine hydrochloride and air-dried under vacuum. Recrystallization from acetonitrile yielded a white, crystalline solid, mp 317-323, dec.

Anal. Calcd for C₂₂H₃₀N₄O₁₂S₂: C, 43.56, H, 4.85; N, 9.24; S, 10.56.

Found: C, 43.20; H, 4.92; N, 9.38; S, 10.15.

IR (Nujol): 1805, 1705, 1320, 1275, 1200, 1150, 1075, 1020, 950, 920, 820, 755, 700, and 660.

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